CRYSTAL STRUCTURE OF HUMAN INTERLEUKIN-22

EINAR NEEDS TO CHECK FIGUREs 4 and 6

This application claims priority to provisional application no. 60/317,937 filed September 10, 2001 and provisional application no. 60/333,150 filed November 27, 2001 both incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

The present invention relates to the fields of molecular biology, protein purification, protein crystallization, X-ray diffraction analysis, three-dimensional-structure determination, rational drug design and molecular modeling of related proteins and mutants. The present invention provides crystallization methods and crystallized human interleukin-22 (IL-22). The crystallized IL-22 is physically analyzed by X-ray diffraction techniques. The resulting X-ray diffraction patterns are of sufficiently high resolution to be useful for determining the three-dimensional structure of IL-22, molecular modeling of related proteins and mutants.

BACKGROUND AND PRIOR ART

1. Interleukins.

The last decade has seen knowledge of the immune system and its regulation expand tremendously. One area of particular research interest has focused on the regulatory proteins and glycoproteins of the immune system. One of the best known families of these regulatory molecules is the cytokines. These are molecules which are involved in the "communication" of cells with each other. The individual members of the cytokine family have been found to be involved in a wide variety of pathological conditions, such as cancer and allergies. Whereas sometimes the cytokines are involved in the pathology of the condition, they are also known as being therapeutically useful.

Interleukins are one type of cytokines. The literature on interleukins is vast. An exemplary, but by no means exhaustive listing of the patents in this area includes U.S.

Patent No. 4,778,879 to Mertelsmann *et al.*; U.S. Patent No. 4,490,289 to Stern; U.S. Patent No. 4,518,584 to Mark *et al.*; and U.S. Patent No. 4,851,512 to Miyaji *et al.*, all of which involve interleukin-2 or "IL-2." Additional patents have issued which relate to interleukin-1 ("IL-1"), such as U.S. Patent No. 4,808,611 to Cosman. The disclosure of all of these patents are incorporated by reference herein. More recent patents on different interleukins include U.S. Patent Nos. 5,694,234 (IL-13); 5,650,492 (IL-12); 5,700,664, 5,371,193 and 5,215,895 (IL-11); 5,728,377, 5,710,251, 5,328,989 (IL-10); 5,580,753, 5,587,302, 5,157,112, 5,208,218 (IL-9); 5,194,375, 4,965,195 (IL-7); 5,723,120, 5,178,856 (IL-6), and 5,017,691 (IL-4). Even a cursory review of this patent literature shows the diversity of the properties of the members of the interleukin family. One can assume that the larger cytokines family shows even more diversity. *See, e.g.*, Aggarwal *et al.*, ed., Human Cytokines: Handbook For Basic And Clinical Research (Blackwell Scientific Publications, 1992); Paul, ed., Fundamental Immunology (Raven Press, 1993), pp. 763-836. All cited references are incorporated by reference herein.

2. Interleukin-9.

The lymphokine IL-9, previously referred to as "P40," is a T-cell derived molecule which was originally identified as a factor that sustained permanent antigen independent growth of T4 cell lines. See, e.g., Uyttenhove *et al.* (1988) *Proc. Natl. Acad. Sci._USA* **85:** 6934; Van Snick *et al.* (1989) *J. Exp. Med.* **169:** 363; Simpson *et al.* (1989) *Eur. J. Biochem.* **183:** 715; all of which are incorporated herein by reference.

IL-9 activity was at first observed on T4-restricted cell lines. IL-9 does not, however, show activity on CTLs or freshly isolated T cells. *See, e.g.*, Uyttenhove *et al.*, *supra*, Schmitt *et al.* (1989) *Eur. J. Immunol.* **19:** 2167. Subsequent experiments demonstrated that T-cell-growth factor III (TCGF III) is identical to mast cell growth enhancing activity (MEA), a factor that potentiates the proliferative response of bone-marrow-derived mast cells to IL-3. Studies on IL-9 have shown that it also supports erythroid colony formation (Donahue *et al.* (1990) *Blood* **75(12):** 2271-2275); promotes the proliferation of myeloid erythroid burst formation (Williams *et al.* (1990) Blood **76:** 306-311); supports clonal maturation of burst-forming-unit-erythrocytes (BFU-E) of

adult and fetal origin (Holbrook *et al.* (1991) *Blood* **77(10):** 2129-2134); and stimulates proliferation of megakaryoblastic leukemia cells (Yang *et al.* (1989) *Blood* **74:** 1880). IL-9 expression has also been implicated in Hodgkin's disease and large cell anaplastic lymphoma (Merz *et al.* (1990) *Blood* **78(8):** 1311-1317). Genetic analyses of mice susceptible or resistant to the development of bronchial hyperresponsiveness have linked the IL-9 gene and its expression to bronchial hyperresponsiveness susceptibility. *See, e.g.*, Nicolaides *et al.* (1997) *Proc. Natl. Acad. Sci. USA* **94:** 13175-13180. Studies with IL-9-transgenic mice demonstrate that increased IL-9 expression produces lung mastocytosis, hypereosinophilia, bronchial hyperresponsiveness and high levels of IgE. *See, e.g.*, Temann *et al.*, *J. Exp. Med.* **188:** 1307-1320, 1998; Godfraind *et al.* (1998) *J. Immunol.* **160:** 3989-3996; McLane *et al.* (1999) *Am. J. Resp. Cell. Mol.* **19:** 713-720. Genetic studies in humans have also linked IL-9 and IL-9R genes to asthma. *See, e.g.*, Doull *et al.* (1996) *Am. J. Respir. Crit. Care Med.* **153:** 1280-1284; Holroyd *et al.* (1998) *Genomics* **52:** 233-235, 1998. In combination, these observations strongly suggest that IL-9 plays a major role in bronchial hyperresponsiveness, asthma and allergies. *See, e.g.*, PCT Application US96/12757 (Levitt, *et al.*), and PCT Application US97/21992 (Levitt, *et al.*), both of which are incorporated herein by reference.

IL-9 is known to affect the levels of other molecules in subjects. *See e.g.*, Louahed *et al.* 1995) *J. Immunol.* **154:** 5061-5070; Demoulin *et al.* (1996) *Mol. Cell. Biol.* **16:** 4710-4716; both of which are incorporated herein by reference. It will be recognized that the molecules affected have their own functions in biological systems. For example, many of the known activities of IL-9 are mediated by activation of STAT transcription factors. *See e.g.*, Louahed *et al.* (1995) *J. Immunol.* **154:** 5061-5070; Demoulin *et al.* (1996) *Mol. Cell. Biol.* **16:** 4710-4716; both of which are incorporated herein by reference. As such, there is continued interest in trying to identify molecules whose presence and/or level is affected by other molecules, such as cytokines.

3. Interleukin-22

Interleukin-22 (IL-22) is a cytokine that is induced by IL-9 in T cells and mast cells. *See, e.g.*, Dumoutier *et al.* (2000) *J. Immunol.* **164:** 1814-1819; WO 00/24758 and

U.S. Application Serial No. 09/419,568, which are all incorporated herein by reference. The induction of IL-22 expression by IL-9 is rapid—within 1 hour. IL-22 is a 20 kDa protein that has an N-terminal hydrophobic signal peptide and shares amino-acid-sequence homology to interleukin-10 (IL-10). In addition, IL-22 binds two receptors that are members of the class-II-cytokine-receptor family. *See, e.g.*, Xie *et al.* (2000) *J. Biol. Chem.* **275:** 31335-31339; Kotenko *et al.* (2001) *J. Biol. Chem.* **276:** 2725-2732. Recent results demonstrate that the functional IL-22 receptor complex consists of two receptor chains, the CRF2-9 (IL22R) chain and the CRF2-4 (IL-10R2 or IL-10Rβ) chain. *See, e.g.*, Xie *et al.* (2000) *J. Biol. Chem.* **275:** 31335-31339; Kotenko *et al.* (2001) *J. Biol. Chem.* **276:** 2725-2732. Interestingly, CRF2-4, which binds an IL-10 homodimer, is a functional component of the IL-10 signaling complex. *See, e.g.*, Temann, *et al.* (1998) *J. Exp. Med.* **188:** 1307-1320. Although this is the first example of the involvement of a class-II-cytokine-receptor in multiple distinct cytokine signaling complexes, sharing of the gamma-common chain is observed in IL-2, IL-4, IL-7, IL-9 and IL-15 receptor complexes. Other members of the class-II-receptor family include the two interferon-γ (IFN-γ) receptor chains (Rα and Rβ), the two chains of the IFN-α/β receptor, and tissue factor. In contrast, the growth hormone (GH) and prolactin receptors, for example, are members of the class-I-cytokine-receptor family.

Human and mouse IL-22 (IL-22 and mIL-22, respectively) comprise 179 amino-acid residues, including four cysteine residues, and share about 79% sequence identity. In contrast, IL-22 shares only 25% sequence identity with human IL-10 (hIL-10), and mIL-22 shares only 22% sequence identity with hIL-10. The regions of highest sequence identity are located in the C-terminal half of IL-22 and hIL-10. The fact that this region is critical for IL-10 activity, suggests that IL-22 and IL-10 share common or related biological activities.

Although IL-22 appears to play a critical role in immune function, *in vivo* studies in mice have demonstrated that lipopolysaccharide (LPS) induces the expression of IL-22 in numerous organs. *See, e.g.*, Dumoutier *et al.* (2000) *Proc. Natl. Acad. Sci. U.S.A.* **97:** 10144-10149. IL-22 also activates signal transducer and activator of transcription factors (STAT), specifically STAT-1 and STAT-3, in several hepatoma cell lines. The stimulation of HepG2-human-hepatoma cells up-regulates the production of acute-phase

reactants such as serum amyloid A, α-1-antichymotrypsin and haptoglobin. *See, e.g.*, Dumoutier *et al.* (2000) *Proc. Natl. Acad. Sci. U.S.A.* **97:** 10144-10149. A similar induction of acute-phase reactants was observed upon injection of IL-22 into mouse liver. These findings suggest that IL-22 plays a role in the inflammatory response. Importantly, the IL-22 gene is located on human chromosome 12q near a cluster of genetic loci linked to asthma. *See, e.g.*, Xie *et al.* (2000) *J. Biol. Chem.* **275:** 31335-31339; Kotenko, *et al.* (2001) *J. Biol. Chem.* **276:** 2725-2732. Thus, these findings, the induction of IL-22 by IL-9, and the association of IL-9 with inflammation and airway hyperreactivity disorders, in combination, implicate IL-22 in the etiology of asthma and allergy.

The present invention discloses a refined three-dimensional structure of IL-22 of sufficient resolution to identify the IL-22 dimerization interface and the specific amino acid residues that are involved in stabilizing the IL-22 dimer. Although both IL-10 and IL-22 form dimers, and IL-10 binds its receptor as a dimer, the present invention demonstrates that IL-22 binds the IL-22 receptor as a monomer. The present invention provides mutant IL-22 wherein the mutation or mutations destabilize the dimer. These IL-22 mutants provide IL-22 in its biologically active form and are useful as therapeutic agents. The three-dimensional structure of IL-22 of the present invention is also of sufficient resolution to allow the identification of the specific amino acids involved in binding the IL-22 receptor. In addition the present invention provides mutant IL-22 wherein the mutation(s) modify the ability of the mutant IL-22 to bind its receptor. Human IL-22 mutants with increased affinity for the IL-22 receptor are therapeutically useful agonists and antagonists. Furthermore, the present invention provides a crystal structure of sufficient quality for use in methods of rational drug design to produce therapeutically relevant molecules.

SUMMARY OF THE INVENTION

The present invention provides methods for identifying a mammalian IL-22 mutant with modified ability to dimerize, said method comprising the steps of: (a) constructing a three-dimensional structure of IL-22 defined by the atomic coordinates shown in Table 4; (b) employing the three-dimensional structure and modeling methods

to identify an amino acid involved in stabilizing a dimer of IL-22; (c) producing a mammalian IL-22 having a mutation at an amino acid identified in (b); and (d) assaying said mutant IL-22 to determine the ability of said mutant to dimerize as compared to an IL-22 control, wherein a difference in dimerization between said mutant and said control is indicative of a modified ability to dimerize. As used herein, "IL-22", "T-cell-inducible factor (TIF)" and "IL-TIF/IL-22" each refer to a cytokine of about 20 kDa that has an N-terminal hydrophobic signal peptide amino acid sequence homology to interleukin 10 (IL-10), and is upregulated by interleukin-9 (IL-9) in T cells and mast cells. *See, e.g.*, Dumoutier *et al.* (2000) *J. Immunol.* **164:** 1814-1819. As used herein, "mammalian IL-22" or "IL-22" refers to a mammalian cytokine of about 20 kDa, which has an N-terminal hydrophobic signal peptide, amino acid sequence homology to interleukin 10 (IL-10), and is upregulated by interleukin-9 (IL-9) in T cells and mast cells. Preferably, mammalian IL-22 is from, for example, human, horses, cows, sheep, goats, cats, dogs, pigs, rats and mice. More preferably, mammalian IL-22 is human IL-22 (IL-22). In a preferred embodiment, "human IL-22" consists of the amino acid sequence of SEQ ID NO: 2.

As used herein, "ability to dimerize" refers to the ability of two IL-22 monomers to form an IL-22 dimer. Mutations that either strengthen inter-monomer contacts or weaken the inter-monomer interactions modify the ability of IL-22 to dimerize. As used herein, "stabilizing the dimer" refers to the effect of an energetically favorable mutation that strengthens inter-monomer contacts. As used herein, an amino acid is "involved" in stabilizing the dimer when the amino acid directly or indirectly contributes to the stability of the dimer—either sterically or through non-covalent bonding (*i.e.* van der Waals interactions, hydrogen bonding, hydrophobic interactions, etc.), and the like. As used herein, "mutation site" refers to a single amino acid of an IL-22. The IL-22 mutant, however, includes IL-22 molecules that contain mutations at one or more mutation sites. As used herein, "mutation" or "mutations" refers to a substitution of one or more amino acids; a deletion of one or more amino acids; or the addition of one or more amino acids. Preferably, a mutation of the present invention is the substitution, deletion or addition of a single amino acid at one or more mutation sites.

In a preferred embodiment, the "mutation site", that is identified by the three-dimensional structure of IL-22 and modeling methods of the present invention, is an amino acid at a position that is at or near the dimerization interface. More preferably, the "mutation site" is one or more amino acids that are located at the dimerization interface. As used herein, "dimerization interface" refers to the contact area between the two monomers of a dimer. In a preferred embodiment, the contact area between the two monomers of a dimer include amino acid positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, at least two of these amino acid positions or all of these amino acid positions of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, at least two of these amino acid positions, or all of these amino acid positions.

The present invention also provides an isolated peptide selected from the group consisting of:

(a) an amino acid sequence consisting essentially of amino acids 61-71 of SEQ ID NO: 2;

(b) an amino acid sequence consisting essentially of amino acids 61-162 of SEQ ID NO: 2;

(c) an amino acid sequence consisting essentially of amino acids 61-169 of SEQ ID NO: 2;

(d) an amino acid sequence consisting essentially of amino acids 162-169 of SEQ ID NO: 2;

(e) an amino acid sequence consisting essentially of amino acids 98-104 of SEQ ID NO: 2; and

(f) an amino acid sequence consisting essentially of amino acids 98-157 of SEQ ID NO: 2.

In a preferred embodiment the amino acid sequence of the isolated peptide contains a mutation at one or more positions corresponding to position 61, 70, 71, 98-104, 154-157, 162, 166, and 169 of SEQ ID NO: 2.

Another embodiment of the present invention provides mimetics of peptides corresponding to Region 1 or Region 2, mimetics of fragments of peptides corresponding to Region 1 or Region 2 that bind an IL-22 receptor or an IL-22 receptor chain CRF2-4 and/or CRF2-9 or mutants of peptides corresponding to Region 1 or Region 2 and/or mutants thereof.

The mimetics of the present invention includes peptide-containing molecules that mimic elements of protein secondary structure. *See e.g.*, Johnson *et al.*, In: Biotechnology And Pharmacy (Pezzuto *et al.*, eds.; Chapman and Hall, New York, (1993); Coligan *et al.* (1991) *Current Protocols in Immunology* **1(2)**: Chapter 5; both incorporated by reference herein. The underlying rationale behind the use of peptide mimetics is that the peptide backbone of proteins exists chiefly to orient amino acid side chains in such a way as to facilitate molecular interactions, such as those of antibody and antigen or receptor and ligand. A peptide mimetic permits molecular interactions similar to the natural molecule. These principles may be used, in conjunction with the principles outline above, to engineer second generation molecules having IL-22-receptor-binding properties that are improved as compared to unmodified IL-22.

As used herein, the terms "peptidomimetic" and "mimetic" is intended to include peptide analogues which serve as appropriate substitutes for peptides in interactions with, for example, receptors. The peptidomimetic must possess not only affinity, but also efficacy and substrate function. That is, a peptidomimetic exhibits functions of a peptide, without restriction of structure to amino acid constituents. Peptidomimetics, methods for their preparation and use are described in Morgan *et al.* (1989). *See e. g.*, Morgan *et al.* In: Ann. Rep. Med. Chem. (Virick F. J., *et al.*, eds.; Academic Press, San Diego, Calif., 1989) pp. 243-253; incorporated by reference herein. Peptidomimetics and the mutant polypeptides of the present invention may also include targeting moieties or molecules that direct the mimetics and polypeptides to specific tissues and cells. Many targeting moieties are known, and include, for example, asialoglycoproteins (*See e.g.*, U.S. Pat. No. 5,166,320 to Wu) and other ligands which are transported into cells via receptor-mediated endocytosis.

Peptide combinatorial libraries are particularly useful for identifying the mimetics of the present invention (Simon *et al.* (1992) *Proc. Natl. Acad. Sci. USA* **89:** 9367; incorporated herein by reference) and can be used to generate chemically diverse libraries of novel molecules. Once the peptide libraries are generated, they can be screened, for example, by using antibodies—polyclonal or monoclonal antibodies—that are specific to the mutant peptides corresponding to Region 1 and Region 2 of an IL-22, or mutant peptides of the present invention. These antibodies may be added to mimetics derived from the peptide libraries. After a period of incubation and a wash to remove unbound antibody, the presence of bound antibody is determined by standard ELISA assays. *See, e.g.*, Harlow & Lane Antibodies: A Laboratory Manual (Cold Spring Harbor Laboratory; Cold Spring Harbor, N.Y., 1988) pg. 553. Wells that do not contain bound antibody indicate the presence of peptide mimetics that bind to the antibody. Methods for identifying active compounds in pools of small molecules include fractionating the pool by reverse phase HPLC or affinity selection/mass spectroscopy. *See, e.g.*, Nedved *et al.* (1996) *Anal. Chem.* **68:** 4228; Zuckermann *et al.* (1994) *J. Med. Chem.* **37:** 2678; both incorporated herein by reference.

As used herein, the term "mimetic", is not limited to peptide-based mimetics or peptidomimetics. As used herein, the term "mimetics", refers to any molecule capable of mimicking IL-22 and the biological properties of IL-22 (*i.e.*, binding activity and/or and inducing a receptor-mediated downstream biological effect characteristic of IL-22). The mimetics of the present invention may be a protein, peptide, or non-peptidyl based organic molecule. Accordingly, the term "mimetic" embraces any substance having IL-22-like activity, regardless of the chemical or biochemical nature thereof. The mimetics of the present invention may be a simple or complex substance produced by a living system or through chemical or biochemical synthetic techniques. A mimetic of the present invention can be a large molecule, *e.g.*, a mutant IL-22 dimer or monomer, as described herein, or a small molecule, *e.g.*, an organic molecule prepared *de novo* according to the principles of rational drug design. The mimetics of the present invention that are based on mutants of IL-22 also include any substance that structurally resembles a solvent-exposed surface epitope of IL-22 and binds an IL-22 receptor or IL-22 receptor chains. Methods of modeling, identifying and producing the mimetics of the

present invention are disclosed in U. S. Patent Nos. 5,835,382; 6,090,609; 6,242,201; 6,251,620; 6,273,598; and 6,303,287; all incorporated herein by reference.

The present invention also provides methods for identifying and producing mimetics of an IL-22 receptor or IL-22 receptor chain comprising the steps of: a) constructing a three-dimensional structure of hIL-22 defined by the atomic coordinates shown in Table 4; b) employing the three-dimensional structure and modeling methods to identify one or more surface accessible amino acids or one or more amino acids involved in receptor binding; c) producing a mimetic that binds or interacts with the IL-22 at one or more amino acids identified in (b); and c) assaying said mimetic to determine the ability of said mimetic to prevent or reduce the binding of IL-22 to an IL-22 receptor or receptor chain as compared o an IL-22 control, wherein a difference in IL-22 binding between said mimetic and said control is indicative of an IL-22 receptor or IL-22 receptor chain mimetic. In a preferred embodiment, the surface accessible amino acids comprise one or more amino acids selected from the group consisting the amino acids listed in Table 5. In another embodiment, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are preferably the amino acids comprising Region 1 and/or Region 2. More preferably, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are selected from the group consisting of the amino acid at a position corresponding to position 61, 70, 71, 162, 166, 169, 98, 99, 100, 101, 102, 103, 104, 154, 155, 156 and 157 of SEQ ID NO: 2.

The present invention also provides a mimetic of an IL-22 receptor or IL-22 receptor chain that is produced by a method comprising the steps of: a) constructing a three-dimensional structure of hIL-22 defined by the atomic coordinates shown in Table 4; b) employing the three-dimensional structure and modeling methods to identify one or more surface accessible amino acids or one or more amino acids involved in receptor binding; c) producing a mimetic that binds or interacts with the IL-22 at one or more amino acids identified in (b); and c) assaying said mimetic to determine the ability of said mimetic to prevent or reduce the binding of IL-22 to an IL-22 receptor or receptor chain as compared o an IL-22 control, wherein a difference in IL-22 binding between said mimetic and said control is indicative of an IL-22 receptor or IL-22 receptor chain mimetic. In a preferred embodiment, the surface accessible amino acids comprise one or

more amino acids selected from the group consisting the amino acids listed in Table 5. In another embodiment, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are preferably the amino acids comprising Region 1 and/or Region 2. More preferably, the one or more amino acids involved in IL-22 receptor or IL-22 receptor chain binding are selected from the group consisting of the amino acid at a position corresponding to position 61, 70, 71, 162, 166, 169, 98, 99, 100, 101, 102, 103, 104, 154, 155, 156 and 157 of SEQ ID NO: 2.

The present invention also provides antibodies or fragments thereof that specifically bind to one or more epitopes in a region comprising an IL-22 dimerization interface and/or a region involved in IL-22 receptor or IL-22 receptor chain binding. In a preferred embodiment, the antibodies of the present invention are polyclonal antibodies. In a more preferred embodiment, the antibodies of the present invention are monoclonal antibodies. The antibodies of the present invention bind one or more epitopes in a region comprising an IL-22 dimerization interface and/or a region involved in IL-22 receptor or IL-22 receptor chain binding and preferably prevent or interfere with the formation of IL-22 dimers and/or prevent or interfere with the binding of IL-22 to an IL-22 receptor or IL-22 receptor chain, respectively. In a preferred embodiment, the one or more epitopes are located in a region comprising the IL-22 dimerization interface. In a more preferred embodiment, the one or more epitopes comprise one or more of the amino acids selected from the group consisting of amino acids corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. In a most preferred embodiment, the one or more epitopes comprise one or more of the amino acids selected from the group consisting of amino acids corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2. In a preferred embodiment, the one or more epitopes are located in a region comprising the IL-22 receptor- or IL-22-receptor-chain-binding domains. In a more preferred embodiment, the one or more epitopes are located in Region 1 and/or Region 2. In a most preferred embodiment, the epitopes in Region 1 comprise one or more of the amino acids at positions corresponding to positions 61, 70, 71, 162, 166, and 169 of SEQ ID

NO: 2. In a most preferred embodiment, the epitopes in Region 2 comprise one or more of the amino acids at positions corresponding to positions 98, 99, 100, 101, 102, 103, 104 154, 155, 156, or157 of SEQ ID NO: 2.

The present invention also provides methods for identifying a mutant of a mammalian IL-22 with modified ability to bind an IL-22 receptor, said method comprising the steps of: (a) constructing a three-dimensional structure of IL-22 defined by the atomic coordinates shown in Table 4; (b) employing the three-dimensional structure and modeling methods to identify an amino acid involved in receptor binding; (c) producing any IL-22 having a mutation at an amino acid identified in (b); and (d) assaying said mutant IL-22 to determine the ability of said mutant to bind to the IL-22 receptor as compared to an IL-22 control, wherein a difference in binding between said mutant and said IL-22 control is indicative of a modified ability to bind the IL-22 receptor. As used herein, "IL-22 control" refers to an unmodified mammalian IL-22 that is identical to the mutant IL-22 prior to incorporation of the mutation.

In a preferred embodiment, the mutation site is located in an IL-22-receptor-binding site. More preferably, the IL-22-receptor-binding site is Region 1 or Region 2. As used herein, "Region 1" refers to the region of IL-22 that is formed by helix A, loop AB and helix F and binds to the IL-22-receptor chain, CRF2-4 and/or CRF2-9. As used herein, "Region 2" refers to the region of IL-22 that is formed by helix C and helix E and binds to the IL-22-receptor chain, CRF2-4. In a more preferred embodiment, the mutation site in Region 1 is selected from one or more of the amino acids at positions corresponding to positions 61, 70, 71, 162, 166, and 169 of SEQ ID NO: 2. In another embodiment, the mutation in site in Region 2 is selected from at least one of the amino acids at positions corresponding to positions 98, 99, 100, 101, 102, 103, 104 154, 155, 156, or157 of SEQ ID NO: 2.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution in Region 1 or Region 2 or a combination thereof. More preferably, the mutant IL-22 comprises a mutation in Region 1 at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, and 179 of SEQ ID NO: 2, and/or a mutation in Region 2 at one or more positions corresponding to positions 98,

99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2. The present invention also contemplates mutant IL-22 molecules that comprise Region 1, wherein the mutant IL-22 comprises a mutation at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, and/or a mutant IL-22 molecule that comprises Region 2, wherein the mutant IL-22 comprises a mutation at one or more positions corresponding to position 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution at an IL-22 dimerization interface. Preferably, the dimerization interface comprises amino acids at positions corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 5, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2.

In another embodiment, the present invention provides a mutant IL-22 comprising at least one amino acid substitution at a IL-22 dimerization interface, wherein the mutation(s) are at a position or positions that stabilize an IL-22 dimer. Preferably, the mutation or mutations are selected from one or more of the group consisting of:

(a) an amino acid at a position corresponding to position 166 or 175 of SEQ ID NO: 2;

(b) an amino acid at a position corresponding to position 57 or 176 of SEQ ID NO: 2;

(c) an amino acid at a position corresponding to position 73 or 83 of SEQ ID NO: 2;

(d) an amino acid at a position corresponding to position 44 or 64 of SEQ ID NO: 2;

(e) an amino acid at a position corresponding to position 168 or 175 of SEQ ID NO: 2;

(f) an amino acid at a position corresponding to position 75 or 176 of SEQ ID NO: 2;

(g) an amino acid at a position corresponding to position 48 or 61 of SEQ ID NO: 2;

(h) an amino acid at a position corresponding to position 44 or 166 of SEQ ID NO: 2;

(i) an amino acid at a position corresponding to position 61 or 179 of SEQ ID NO: 2; and

(j) an amino acid at a position corresponding to position 49 or 61of SEQ ID NO: 2.

More preferably, the mutation is at one or more amino acid positions corresponding to position 175 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 176 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine, lysine, asparagine and glutamine; position 73 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 44 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 64 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 168 of SEQ ID NO: 2; wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 61 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamate, glutamine, asparagine, serine, threonine and cysteine; and position 49 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamine, asparagine, glutamate and aspartate.

The present invention also provides isolated polynucleotides that encode a mutant IL-22 comprising at least one amino acid substitution in Region 1 or Region 2. More preferably, the polynucleotides encode the mutant IL-22 that comprises a mutation in Region 1 at one or more positions corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, and 179 of SEQ ID NO: 2, and/or a mutation in Region 2 at

one or more positions corresponding to positions 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2. The present invention also contemplates polynucleotides that encode mutant IL-22 molecules that comprise Region 1, wherein the mutant IL-22 comprises at least one mutation at a position corresponding to position 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2, and/or a mutant IL-22 molecule that comprises Region 2, wherein the mutant IL-22 comprises at least one mutation at a position corresponding to position 98, 99, 100, 101, 102, 103, 104, 154, 155, 156, or 157 of SEQ ID NO: 2.

In another embodiment, the isolated polynucleotides encode mutant IL-22 comprising at least one amino acid substitution at a IL-22 dimerization interface. Preferably, the dimerization interface comprises amino acids at positions corresponding to positions 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, or 179 of SEQ ID NO: 2. More preferably, the dimerization interface comprises amino acids at positions corresponding to positions 44, 48, 49, 57, 61, 64, 73, 75, 83, 166, 168, 175, 176, or 179 of SEQ ID NO: 2.

In another embodiment, the present invention provides isolated polynucleotides that encode a mutant IL-22 comprising at least one amino acid substitution at an IL-22 dimerization interface, wherein the mutation or mutations are at a position or positions that stabilize an IL-22 dimer. Preferably, the mutation or mutations are selected from one of more of the group consisting of:

(a) an amino acid at a position corresponding to position 166 or 175 of SEQ ID NO: 2;

(b) an amino acid at a position corresponding to position 57 or 176 of SEQ ID NO: 2;

(c) an amino acid at a position corresponding to position 73 or 83 of SEQ ID NO: 2;

(d) an amino acid at a position corresponding to position 44 or 64 of SEQ ID NO: 2;

(e) an amino acid at a position corresponding to position 168 or 175 of SEQ ID NO: 2;

(f) an amino acid at a position corresponding to position 75 or 176 of SEQ ID NO: 2;

(g) an amino acid at a position corresponding to position 48 or 61 of SEQ ID NO: 2;

(h) an amino acid at a position corresponding to position 44 or 166 of SEQ ID NO: 2;

(i) an amino acid at a position corresponding to position 61 or 179 of SEQ ID NO: 2; and

(j) an amino acid at a position corresponding to position 49 or 61of SEQ ID NO: 2.

More preferably, the isolated polynucleotides encode an IL-22 mutant, wherein the mutation is at one or more amino acid positions corresponding to position 175 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 176 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine, lysine, asparagine and glutamine; position 73 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 44 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 64 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 168 of SEQ ID NO: 2; wherein the substitution is any amino acid except glutamate, aspartate, glutamine, asparagine, serine, threonine and cysteine; position 61 of SEQ ID NO: 2, wherein the substitution is any amino acid except arginine and lysine; position 166 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamate, aspartate, glutamate, glutamine, asparagine, serine, threonine and cysteine; and position 49 of SEQ ID NO: 2, wherein the substitution is any amino acid except glutamine, asparagine, glutamate and aspartate.

The present invention also provides a mutant IL-22 comprising at least one amino acid substitution at one or more glycosylation sites, wherein the substitution prevents or reduces the glycosylation of IL-22. In a preferred embodiment, the at least one amino

acid substitution is at a position selected from the group consisting of amino acid positions corresponding to position 54, 55, 56, 97, 98 or 99 of SEQ ID NO: 2. In a more preferred embodiment, the at least one amino acid substitution corresponds to position 54, 56, 97, or 99 of SEQ ID NO: 2, or a combination thereof.

In another embodiment, the mutant IL-22 comprises one or more amino acid substitutions, wherein the substitution or substitutions produce a glycosylation site at the dimerization interface. In a preferred embodiment, the glycosylation site consists of the amino acid sequence Asn-Xaa-Thr/Ser. In one embodiment, insertion of a glycosylation site increases the glycosylation of IL-22. In another embodiment, insertion of a glycosylation site increases the glycosylation of IL-22 and prevents or reduces the dimerization of IL-22 as compared to an unsubstituted IL-22.

In another embodiment, a mutant IL-22 of the present invention comprising a mutation in Region 1, Region 2, or at the dimerization interface, further comprises one or more amino acid substitutions, wherein the substitution or substitutions produce a glycosylation site at the dimerization interface. In a preferred embodiment, the glycosylation site consists of the amino acid sequence Asn-Xaa-Thr/Ser. In one embodiment, insertion of a glycosylation site increases the glycosylation of IL-22. In another embodiment, insertion of a glycosylation site increases the glycosylation of IL-22 and prevents or reduces the dimerization of IL-22 as compared to an unsubstituted IL-22.

The present invention also provides a computer system comprising: a) a memory comprising atomic coordinates shown in Table 4; and b) a processor in electrical communication with the memory; wherein the processor generates a molecular model having a three dimensional shape representative of at least a portion of a mammalian IL-22. In a preferred embodiment, the atomic coordinates shown in Table 4 are stored on a computer readable diskette.

The present invention also provides cloning and expression vectors that comprise the polynucleotides of the present invention. In another embodiment, host cells are transformed with the vectors of the present invention and are used in methods of

producing the encoded mutant IL-22 that comprise culturing the host cells and isolating the mutant IL-22.

The present invention also provides pharmaceutical compositions comprising the mutant IL-22, peptides or mimetics of the present invention and a pharmaceutically acceptable carrier. As used herein, "pharmaceutically acceptable carrier" refers to any carrier, solvent, diluent, vehicle, excipient, adjuvant, additive, preservative, and the like, including any combination thereof, that is routinely used in the art.

Physiological saline solution, for example, is a preferred carrier, but other pharmaceutically acceptable carriers are also contemplated by the present invention. The primary solvent in such a carrier may be either aqueous or non-aqueous. The carrier may contain other pharmaceutically acceptable excipients for modifying or maintaining pH, osmolarity, viscosity, clarity, color, sterility, stability, rate of dissolution, and/or odor. Similarly, the carrier may contain still other pharmaceutically acceptable excipients for modifying or maintaining the stability, rate of dissolution, release, or absorption or penetration across the blood-brain barrier.

The pharmaceutical compositions of the present invention may be administered orally, topically, parenterally, rectally or by inhalation spray in dosage unit formulations that contain conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles. As used herein, "parenterally" refers to subcutaneous, intravenous, intramuscular, intrasternal, intrathecal, and intracerebral injection, including infusion techniques.

The pharmaceutical compositions may be administered parenterally in a sterile medium. The compositions, depending on the vehicle and concentration used, may be

suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle. The most preferred route of parenteral administration of the pharmaceutical compositions of the present invention is subcutaneous, intramuscular, intrathecal or intracerebral. Other embodiments of the present invention encompass administration of the composition in combination with one or more agents that promote penetration of active ingredients across the blood-brain barrier, and/or slow-release of the active ingredient(s). Such excipients include those substances usually and customarily used to formulate dosages for parenteral administration in either unit dose or multi-dose form or for direct infusion into the CSF by continuous or periodic infusion from an implanted pump.

The desired or optimal dose of the compositions of the present invention may be obtained by parenteral administration that is repeated daily, more frequently, or less frequently. The compositions may also be infused continuously or periodically from an implanted pump. The frequency of dosing will depend on the pharmacokinetic parameters of the specific mutant IL-22, peptide or mimetic in the formulation and the route of administration.

In more preferred embodiments, the pharmaceutical compositions are administered as orally active formulations, inhalant spray or suppositories. The pharmaceutical compositions of the present invention may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, syrups or elixirs.

Active ingredient may be combined with the carrier materials in an amount to produce a single dosage form. The amount of the active ingredient will vary, depending

upon the identity of the mutant, peptide, or mimetic, the host treated, and the particular mode of administration.

Regardless of the manner of administration, however, the specific dose is calculated according to approximate body weight or body surface area of the patient. Further refinement of the dosing calculations necessary to optimize dosing for each of the contemplated formulations is routinely conducted by those of ordinary skill in the art without undue experimentation, especially in view of the dosage information and assays disclosed herein.

The present invention also provides a method of treating a subject in need of IL-22, comprising the step of administering one of the pharmaceutical composition of the present invention, wherein the pharmaceutical composition is an IL-22-receptor agonist.

The present invention also provides a method of inhibiting IL-22 in a subject in need thereof, comprising the step of administering one of the pharmaceutical composition of the present invention, wherein the pharmaceutical composition inhibits the activation of an IL-22 receptor by IL-22.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. (A) Stereoview of the C_α trace of the dimeric structure of IL-22. **(B)** Schematic representation of the secondary structure of IL-22 monomer A, according to PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26:** 283-291; Polikarpov *et al.* (1997) *Nucl. Instrum. Methods* **405:** 159-164), showing the location of the two disulfide bonds (Cys40-Cys132 and Cys89-Cys178). The figures were prepared using Molscript (Dauter, *et al.* (2000) *Acta Cryst.* **D56:** 232-237), Bobscript (Nagem *et al.* (2001) *Acta Cryst.* **D57:** 996-1002) and Raster3D (Perrakis *et al.* (1999) *Nature Struct. Biol.* **6:** 458-463).

Figure 2. Least-square fit of monomer A to monomer B. The root-mean-square deviation (rmsd) is shown as a function of residue numbers. Only main chain atoms were used in calculation.

Figure 3. Contact surface of the IL-22 dimer, shaded according to residue hydrophobicity **(A,B)** and electrostatic potential **(C,D)**. **(A,C)** show the interface of monomer A, whereas **(B,D)** show the interface of monomer B. In parts **(A)** and **(B)** the darker the stippled shading the greater the hydrophobicity. In parts **(C)** and **(D)** areas of negative, positive and neutral electrostatic potential are in medium stippling, dark stippling and light or no stippling, respectively. The figures were prepared with GRASP. *See, e.g.*, Brünger, *et al.* (1998) *Acta Cryst.* **D54:** 905-921.

Figure 4. Secondary structure diagram showing the superposition of an IL-22 monomer (in medium stippling) onto **(A)** a hIL-10 dimer (from helices A to D in dark stippling and from helices E′ to F′ in light stippling; helices A′ to D′, E and F were omitted) and **(B)** a hIFN-γ dimer (from helices A to D in light stippling and from helix E′ to F′ in black; helices A′ to D′, E and F were omitted). Superposition of an IL-22 dimer (in dark stippling and no stippling) onto **(C)** a hIL-10 dimer (in black and light stippling) and **(D)** a hIFN-γ dimer (in medium stippling and light stippling).

Figure 5. Primary structure alignment of murine, and human IL-22 (SEQ ID NO: 3 and 2 respectively) and human IL-10 (SEQ ID NO: 1). Whenever possible, the three dimensional information was used to improve alignment. Disulfide bonds in IL-22 are marked with filled-in circles. The amino acid similarity between IL-22 and hIL-10, as calculated by the program ALSCRIPT (Nicholls *et al.* (1991) *Struct. Funct. Genet.* 11: 281-296), are boxed. Residues conserved in mIL-22 and IL-22 are boxed in the sequence of mIL-22. The loops and helices of human IL-22's secondary structure are depicted. The figure was drawn using the program ALSCRIPT (Nicholls *et al.* (1991) *Struct. Funct. Genet.* 11: 281-296).

Figure 6. **(A)** Superposition of the hIFN-γ/hIFN-γRα complex (hIFN-γ light stippling and medium stippling; hIFN-γRα normal) onto IL-22 monomer (dark stippling). Superposition of **(B)** hIFN-γ (light stippling and darkest stippling) and **(C)**

hIL-10 (darkest stippling and light stippling) onto IL-22 in a coil representation of the potential receptor binding site of IL-22 (medium stippling). Residues involved in direct interaction with a receptor chain are also shown.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides methods for crystallizing human interleukin-22. The resultant crystals diffract X-rays with sufficiently high resolution to allow determination of the atomic coordinates and solve the three-dimensional structure of IL-22. The three-dimensional structure, as provided on computer-readable media described herein, is useful for rational drug design of IL-22-related mimetics, IL-22 mutants and ligands of the IL-22 receptor. Such mimetics, mutants and ligands are useful for treating and inhibiting IL-22-mediated processes or IL-22-related disorders and diseases such as asthma, inflammation and cancer.

1. IL-22 Crystallization.

The isolation and purification of human IL-22, including polynucleotides, vectors and transformed or transfected host cells encoding IL-22, and recombinant methods of IL-22 production, are described in WO 00/24758 and U.S. Application Serial No. 09/419,568, which are both incorporated herein in their entirety. The amino acid sequences of mouse IL-22, human IL-22 and human IL-10 are presented in Figure 5 as SEQ ID NO: 3, 2, and 1, respectively.

Recombinant IL-22 of the present invention may be produced by the following process or other recombinant protein expression methods:

a. constructing, by conventional molecular-biology methods, an expression vector comprising an operon that encodes IL-22, thereby producing a vector for the expression of IL-22;

b. transferring the expression vectors to a host cell by conventional molecular biology methods to produce a transfected or transformed host cell for the expression of IL-22; and

c. culturing the transfected or transformed cell by conventional molecular-biology methods so as to produce IL-22.

The IL-22 of the present invention may be produced using conventional molecular-biology methods. The term "conventional molecular biology methods" refers to techniques for manipulating polynucleotides that are well known to the person of ordinary skill in the art of molecular biology. Examples of such well known techniques can be found in Sambrook *et al.* Molecular Cloning: A Laboratory Manual, 3rd Edition (Cold Spring Harbor, N.Y.; 2001). Examples of conventional molecular biology techniques include, but are not limited to, *in vitro* ligation, restriction-endonuclease digestion, PCR, cellular transformation and transfection, hybridization, electrophoresis, DNA sequencing, and the like.

Specifically, the general methods for construction of the vector of the invention, transfection of cells to produce the host cell of the invention, and culturing of cells to produce the IL-22 of the present invention are all conventional molecular biology methods. Likewise, once produced, the IL-22 of the present invention may be purified by standard procedures of the art, including ammonium-sulfate precipitation, affinity-column chromatography, gel electrophoresis and the like.

The present invention also provides polynucleotide vectors for the replication, manipulation and expression of the isolated polynucleotides of the present invention. Preferably, the vectors allow expression of the isolated polynucleotides of the present invention in either prokaryotic or eukaryotic cells. Prokaryotic cells are selected from bacterial cells, *e.g. Escherichia coli*, and eukaryotic cells are selected from insect, fungal, *e.g. Saccharomyces, Pichia pastoris*, and mammalian cells, *e.g.* Chinese hamster ovary (CHO) and human. The vectors of the present invention may contain regulatory elements that allow inducible or constitutive expression of the operably-linked polynucleotide, confer antibiotic resistance, improve secretion, purification and detection, *e.g.* His and antigen tags, and the like.

The host cells may be either a bacterial cell such as *Escherichia coli*, or a eukaryotic cell. Mammalian cells such as Chinese hamster ovary cells, may also be

used. Notably, the choice of expression vector is dependent upon the choice of host cell, and may be selected so as to have the desired expression and regulatory characteristics in the selected host cell.

The first prerequisite for solving the three-dimensional structure of a protein by X-ray crystallography is a well-ordered crystal that will strongly diffract X-rays. X-rays are directed onto a regular, repeating array of identical molecules so that the X-rays are diffracted from it in a pattern from which the structure of an individual molecule can be retrieved. Different crystal forms can be more or less well-ordered and hence give diffraction patterns of different quality. As a general rule, the more closely the protein molecules pack, and consequently the less water the crystals contain, the better is the diffraction pattern because the molecules are better ordered in the crystal. Well-ordered crystals of globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and crystals thereof contain large holes or channels that are formed between the individual molecules. These channels, which usually occupy more than half the volume of the crystal, are filled with disordered solvent molecules. The protein molecules are in contact with each other at only a few small regions. This is one reason why structures of proteins determined by X-ray crystallography are generally the same as those for the proteins in solution.

The formation of crystals is dependent on a number of different parameters, including pH, temperature, protein, concentration, the nature of the solvent and precipitant, as well as the presence of added ions or ligands. Crystallization experiments may be needed to screen all these parameters for the few combinations that might give crystals suitable for X-ray diffraction analysis. Crystallization robots can automate and speed up the work of reproducibly setting up large number of crystallization experiments.

A pure and homogeneous protein sample is important for successful crystallization. Proteins obtained from cloned genes in efficient expression vectors can quickly be purified to homogeneity in large quantities in a few purification steps. A protein to be crystallized is preferably at least 93-99% pure, according to standard criteria of homogeneity. Crystals form when molecules are precipitated very slowly from

supersaturated solutions. The most frequently used procedure for making protein crystals is the hanging-drop method, in which a drop of protein solution is brought very gradually to supersaturation by loss of water from the droplet to the larger reservoir that contains salt or polyethylene glycol solution.

In general, IL-22 is purified as described in WO 00/24758 and U.S. Application Serial No. 09/419,568, which are both incorporated herein by reference. The resulting IL-22 is in sufficiently pure and concentrated for crystallization. The purified IL-22 preferably runs as a single band under reducing or nonreducing polyacrylamide gel electrophoresis (PAGE) (nonreducing conditions are used to evaluate the presence of disulfide bonds). Purified IL-22 is preferably crystallized using the hanging drop method under varying conditions of at least one of the following: pH, buffer type, buffer concentration, salt type, polymer type, polymer concentration, other precipitating agents and concentration of purified and cleaved IL-22. *See, e.g.*, the methods provided in a commercial kit, such as CRYSTAL SCREEN (Hampton Research, Riverside, Calif.); Taylor *et al.* (1992) *J. Mol. Biol.* 226:1287-1290; Takimoto *et al.* (1992), *infra*.

Crystallization conditions suitable to produce diffraction-quality crystals may be selected from a buffer containing, for example: between 1 and 100 mg/ml IL-22 in 10-200 mM buffer (pH 4-9) (*e.g.*, phosphate, cacodylate, acetates, imidazole, Tris HCl, sodium HEPES); and optionally a salt (*e.g.*, calcium chloride, sodium citrate, magnesium chloride, ammonium acetate, ammonium sulfate, potassium phosphate, magnesium acetate, zinc acetate; calcium acetate); and optionally 0-50% of a polymer (*e.g.*, polyethylene glycol (PEG); average molecular weight 200-10,000); and optionally other precipitating agents (salts: potassium or sodium tartrate, ammonium sulfate, sodium acetate, lithium sulfate, sodium formate, sodium citrate, magnesium formate, sodium phosphate, potassium sulfate, ammonium phosphate); and optionally organics *e.g.*, 2-propanol; non-volatile: 2-methyl-2,4-pentanediol).

The above mixtures are used and screened by varying at least one of pH, buffer type; buffer concentration, precipitating salt type or concentration, PEG type, PEG concentration, and protein concentration. Crystals ranging in size from 0.2-0.7 mm are formed in 1-7 days. From one to ten crystals are observed in one drop and crystal forms,

such as, but not limited to, bipyramidal, rhomboid, and cubic, are suitable. Initial X-ray analyses indicate that such crystals diffract at moderately high to high resolution. When fewer crystals are produced in a drop, they can be much larger size, *e.g.*, 0.4-0.9 mm. These crystals diffract X-rays to at least 3.5 Å resolution, such as 1.5-3.5 Å, or any range of value therein, such as 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, or 3.0, with 3.0 Å or less being preferred.

2. X-ray Diffraction and Structure Determination.

The X-ray diffraction patterns of the invention are of sufficiently high resolution for three-dimensional modeling of IL-22 and IL-22-related molecules, such as IL-22-receptor ligands and IL-22-receptor-chain mimics. Preferably the resolution is in the range of 1.5 to 3.5 Å, more preferably 1.5-3.0 Å and most preferably about 1.9 Å.

X-rays may be produced by high-voltage tubes in which an anode emits X-rays of a specific wavelength upon bombardment by accelerating electrons. More powerful X-ray beams can be produced in synchrotron storage rings where electrons (or positrons) travel near the speed of light. These particles emit very strong radiation at all wavelengths—from short gamma rays to visible light. When used as an X-ray source, however, only X-ray radiation is channeled from the storage ring. Polychromatic X-ray beams are produced by having a broad window that allows through X-ray radiation with wavelengths of 0.2-3.5 Å.

In diffraction experiments, a narrow and parallel beam of X-rays is taken out from the X-ray source and directed onto the crystal to produce diffracted beams. The incident primary beam causes damage to both protein and solvent molecules. The crystal is, therefore, usually cooled to prolong its lifetime (*e.g.*, -220 to -50 C). The primary beam must strike the crystal from many different directions to produce all possible diffraction spots, and so the crystal is rotated in the beam during the experiment.

The diffracted spots are recorded either on a film, the classical method, or by an electronic detector. The exposed film is measured and digitized by a scanning device, whereas electronic detectors feed the signals they detect directly in a digitized form into

a computer. Electronic area detectors significantly reduce the time required for data collection.

When the primary beam from an X-ray source strikes the crystal, some of the X-rays interact with the electrons on each atom and cause them to oscillate. The oscillating electrons serve as a new source of X-rays, which are emitted in almost all directions, referred to as scattering. When atoms and their electrons are arranged in a regular three-dimensional array, the X-rays emitted from the oscillating electrons interfere with one another. In most cases, these X-rays, colliding from different directions, cancel each other out; those from certain directions, however, will add together to produce diffracted beams of radiation that can be recorded as a pattern on a photographic plate or detector.

The diffraction pattern obtained in an X-ray experiment is related to the crystal that caused the diffraction. X-rays that are reflected from adjacent planes travel different distances, and diffraction only occurs when the difference in distance is equal to the wavelength of the X-ray beam. This distance is dependent on the reflection angle, which is equal to the angle between the primary beam and the planes.

The relationship between the reflection angle (θ), the distance between the planes (d), and the wavelength (λ) is given by Bragg's law: $2d\sin\theta.\lambda$. This relationship can be used to determine the size of the unit cell in the crystal. Briefly, the position on the film of the diffraction data relates each spot to a specific set of planes through the crystal. By using Bragg's law, these positions can be used to determine the size of the unit cell.

Each atom in a crystal scatters X-rays in all directions, and only those that positively interfere with one another, according to Bragg's law, give rise to diffracted beams that can be recorded as a distinct diffraction spot above background. Each diffraction spot is the result of interference of all X-rays with the same diffraction angle emerging from all atoms. For the protein crystal of myoglobin, for example, each of the about 20,000 diffracted beams that have been measured contain scattered X-rays from each of the around 1500 atoms in the molecule. To extract information about individual atoms from such a system requires considerable computation. The mathematical tool that is used to handle such problems is called the Fourier transform.

Each diffracted beam, which is recorded as a spot on the film, is defined by three properties: the amplitude, which we can measure from the intensity of the spot; the wavelength, which is set by the X-ray source; and the phase, which is lost in X-ray experiments. All three properties are needed for all of the diffracted beams, in order to determine the position of the atoms giving rise to the diffracted beams.

For larger molecules, protein crystallographers have determined the phases in many cases using a method called multiple isomorphous replacement (MIR) (including heavy metal scattering), which requires the introduction of new X-ray scatterers into the unit cell of the crystal. These additions are usually heavy atoms that contribute significantly to the diffraction pattern. Since such heavy metals contain many more electrons than the carbon, hydrogen, oxygen, nitrogen and sulfur atoms of the protein, they scatter X-rays more strongly. All diffracted beams would therefore increase in intensity after heavy-metal substitution if all interference were positive. In fact, however, some interference is negative; consequently, following heavy-metal substitution, some spots measurably increase in intensity, others decrease, and many show no detectable difference. Isomorphous replacement is usually done by diffusing different heavy-metal complexes into the channels of the preformed protein crystals. The protein molecules expose side chains (such as SH groups) into these solvent channels that are able to bind heavy metals. It is also possible to replace endogenous light metals in metalloproteins with heavier ones, *e.g.*, zinc by mercury, or calcium by samarium.

Phase differences between diffracted spots can be determined from intensity changes following heavy-metal substitution. First, the intensity differences are used to deduce the positions of the heavy atoms in the crystal unit cell. Fourier summations of these intensity differences give maps of the vectors between the heavy atoms—the so-called Patterson maps. From these vector maps the atomic arrangement of the heavy atoms is deduced. From the positions of the heavy metals in the unit cell, one can calculate the amplitudes and phases of their contribution to the diffracted beams of protein crystals containing heavy metals.

This knowledge is then used to find the phase of the contribution from the protein in the absence of the heavy-metal atoms. As both the phase and amplitude of the heavy

metals, the amplitude of the protein alone, and the amplitude of the protein plus heavy metals is known, one phase and three amplitudes are known. From this, the interference of the X-rays scattered by the heavy metals and protein can be calculated to see if it is constructive or destructive. The extent of positive or negative interference, with knowledge of the phase of the heavy metal, gives an estimate of the phase of the protein. Because two different phase angles are determined and are equally good solutions, a second heavy-metal complex can be used which also gives two possible phase angles. Only one of these will have the same value as one of the two previous phase angles; it therefore represents the correct phase angle. In practice, more than two different heavy-metal complexes are usually made in order to give a reasonably good phase determination for all reflections. Notably, each individual phase estimate contains experimental errors arising from errors in the measured amplitudes, and for many reflections, the intensity differences are too small to measure after one particular isomorphous replacement.

The amplitudes and the phases of the diffraction data from the protein crystals are used to calculate an electron-density map of the repeating unit of the crystal. This map then has to be interpreted as a polypeptide chain with a particular amino acid sequence. The interpretation of the electron-density map is complicated by several limitations of the data. First of all, the map itself contains errors, mainly due to errors in the phase angles. In addition, the quality of the map depends on the resolution of the diffraction data, which depends on crystal quality and degree of order. This directly influences the image that can be produced. The resolution is measured in Ångstrom units—as this number decreases, the resolution increases and consequently, the amount of molecular detail observed also increases.

Building the initial model begins by determining how the polypeptide chain weaves its way through the electron-density map. The resulting chain trace constitutes a hypothesis, by which one tries to match the density of the side chains to the known sequence of the polypeptide. When a reasonable chain trace has finally been obtained, an initial model is built to give the best fit of the atoms to the electron density. Computer graphics are used both for chain tracing and for model building to present the data and manipulate the models.

The initial model will contain some errors. Provided the protein crystals diffract to a sufficiently high resolution—better than 3.5 Å—most or substantially all of the errors can be removed by crystallographic refinement of the model using computer algorithms. In this process, the model is modified to minimize the difference between the experimentally observed diffraction amplitudes and those calculated for a hypothetical crystal containing the model, instead of the real molecule. This difference is expressed as an R factor (residual disagreement), which is 0.0 for exact agreement and about 0.59 for total disagreement.

In general, the R factor is preferably between 0.15 and 0.35, and more preferably between about 0.24-0.28 for a well-determined protein structure. The residual difference is a consequence of errors and imperfections in the data. These derive from various sources, including slight variations in the conformation of the protein molecules, as well as inaccurate corrections both for the presence of solvent and for differences in the orientation of the microcrystals from which the crystal is built. This means that the final model represents an average of molecules that are slightly different both in conformation and orientation. In refined structures at high resolution, there are usually no major errors in the orientation of individual residues, and the estimated errors in atomic positions are usually around 0.1-0.2 Å, provided the amino acid sequence is known. Hydrogen bonds, both within the protein and to bound ligands, can be identified with a high degree of confidence.

Most X-ray structures are determined to a resolution between 1.7 Å and 3.5 Å. Electron-density maps with this resolution range are preferably interpreted by fitting the known amino acid sequences into regions of electron density in which individual atoms are not resolved.

The IL-22 crystals are analyzed using a suitable X-ray source and diffraction patterns are obtained. Crystals are preferably stable for at least 10 hrs in the X-ray beam. Frozen crystals (*e.g.*, -220 to -50 C) could also be used for longer X-ray exposures (*e.g.*, 24-72 hrs), the crystals being relatively more stable to the X-rays in the frozen state. To collect the maximum number of useful reflections, multiple frames are optionally collected as the crystal is rotated in the X-ray beam, *e.g.*, for 24-72 hrs. Larger crystals

(>0.2 mm) are preferred, to increase the resolution of the X-ray diffraction. Alternatively, crystals may be analyzed using a synchrotron high-energy X-ray source. Using frozen crystals, X-ray diffraction data is collected on crystals that diffract to a relatively high resolution of 3.5 Å or less, sufficient to solve the three-dimensional structure of IL-22 in considerable detail, as presented herein. Specifically, crystals were soaked in different cryosoaking solutions, mounted in a rayon loop and finally flash-cooled to 80 K in a cold nitrogen stream. Data collection was performed at the Protein Crystallography beamline (LNLS, Campinas, Brazil; Polikarpov *et al.* (1997) *J. Synchrotron Rad.* **5:** 72-76; Polikarpov *et al.* (1997) *Nucl. Instrum. Methods A* **405:** 159-164) and at the X4A beamline (NSLS, Upton, USA), using a MAR345 image plate and a Quantum-4 CCD detector.

The heavy metal derivatives are used to determine the phase, *e.g.,* by the isomorphous replacement method. Heavy atom isomorphous derivatives of IL-22 are used for X-ray crystallography, where the structure is solved using one or several derivatives, which, (when combined) improves the overall figure of merit. Derivatives are identified through Patterson maps and/or cross-phase difference Fourier maps, *e.g.,* using commercially-available software, including the CCP4 package (SERC Collaborative Computing Project No. 4, Daresbury Laboratory, UK, 1979); SIRAS; SHARP [35]; DREAR [31] and SnB 2.1 [32]; and SOLOMON [36]. The program MLPHARE (Wolf *et al.*, eds., Isomorphous Replacement and Anomalous Scattering: Proceedings of CCP4 Study Weekend, pp. 80-86, SERC Daresbury Lab., UK (1991)) is optionally used for refinement of the heavy atom parameters and the phases derived from them by comparing at least one of completeness (%), resolution (in Å), R^r (%), heavy atom concentration (mM), soaking time, heavy atom sites, phasing power (acentric, centric). Addition of heavy atom derivatives produce an MIR map with recognizable features.

Once the initial phases are calculated to 3.2 Å, they may be improved and extended to a higher resolution of 2.8 Å, using solvent flattening, histogram matching and/or Sayre's equation in the program DM. *See e.g.*, Cowtan *et al.* (1993) *Acta Crystallogr.* **49:** 148-157. The skeletonization of the DM procedure is optionally used to improve connectivity in the bulk of the protein envelope. Both the MIR and density

modified maps are optionally used in subsequent stages, to provide sufficient resolution and/or modeling of surface structures.

Skeletonized representations of electron density maps are then computed. These maps are automatically or manually edited using suitable software, *e.g.*, the graphics package FRODO (Jones *et al.* (1991), *infra*) to give a continuous C_α trace. The IL-22 sequence is then aligned to the trace. Initially pieces of idealized polypeptide backbone were placed into regions of the electron density map with obvious secondary structures (*e.g.*, α-helix, β-sheet). After a polyalanine model was constructed for the protein, amino acid side-chains were added where density was present in the maps. The amino acid sequence of IL-22 was then examined for regions with distinct side-chain patterns (*e.g.*, three consecutive aromatic rings). When a pattern in the sequence was found to match an area of the map, the correct side-chains were built onto the existing model. Eventually fragments containing recognizable sequence motifs were connected into a single chain, completing the tracing of the amino acid sequence into the maps. Cycles of simulated annealing against these data may be refined using the program X-PLOR for molecular dynamics for R-factor refinement. *See e.g.*, Brünger *et al.* (1987) *J. Mol. Biol.* **203:** 803-816. This refinement was followed by manual rebuilding with FRODO using experimental and $2F_o$ -F_c maps. The model may be further refined using a least- squares refinement program, such as TNT. *See e.g.*, Tronrud *et al.* (1987) *Acta Crystallogr.* **A 43:** 489-501. One or more of the above modeling steps may performed to provide a molecular 3-D model of IL-22. It is preferred that the IL-22 model has no residues in disallowed regions of the Ramachandran plot, and gives a positive 3D-1D profile (Luthy *et al.* (1992) *Nature* **356:** 83-85; Kraulis (1991), *infra*), suggesting that all the residues are in acceptable environments.

Alternatively, a program such as ARP (Lamzin *et al.* (1993) *Acta Cryst.* **D49:** 129-147) may be used to add crystallographic waters and as a tool to check for bad areas in the model. The programs PROCHECK (Lackowski *et al.* (1993) *J. Appl. Cryst.* **26:** 283-291), WHATIF (Vriend (1990) *J. Mol. Graph.* **8:** 52-56), PROFILE 3D (Luthy *et al.* (1992) *Nature* **356:** 83-85), and ERRAT (Colovos *et al.* (1993) *Protein Science* **2:** 1511-1519), as well as the geometrical analysis generated by X-PLOR were used to check the structure for errors. Anisotropic scaling between F_{obs} and F_{calc} may be applied

after careful assessment of the quality and completeness of the data. The program DSSP may be used to assign the secondary structure elements (Kabsch *et al.* (1983) *Biopolymers* **22:** 2577-2637). A program such as SUPPOS (from the BIOMOL crystallographic computing package) can be used for some or all of the least-squares superpositions of various models and parts of models. The program ALIGN (Cohen (1986) *J. Mol. Biol.* **190:** 593-604) may be used to superimpose N- and C-terminal domains of IL-22. Solvent accessible surfaces and electrostatic potentials can be calculated using such programs as GRASP (Nicholls *et al.* (1991), *infra*).

3. Rational Drug Design and Molecular Modeling of IL-22 and IL-22-Related Proteins.

Three-dimensional modeling is performed using the diffraction coordinates from the X-ray diffraction patterns and atomic coordinates of the present invention. The coordinates are entered into one or more computer programs for molecular modeling, as known in the art. Such molecular modeling can utilize known X-ray diffraction molecular modeling algorithms or molecular modeling software to generate atomic coordinates corresponding to the three-dimensional structure of at least one IL-22 or a fragment thereof.

The entry of the coordinates of the X-ray diffraction patterns and the amino acid sequence into such programs results in the calculation of the most probable secondary, tertiary and quaternary structures of the protein, including overall atomic coordinates of a IL-22 or a fragment thereof. These structures are combined and refined by additional calculations using such programs to determine the probable or actual three-dimensional structure of the IL-22, including potential or actual active or binding sites of the protein.

Such molecular modeling and related programs useful for rational drug design of ligands or mimetics, are contemplated by the present invention. The drug design uses computer modeling programs which calculate how different molecules interact with the various sites of the IL-22, how IL-22 monomers interact with other IL-22 monomers, how IL-22 interacts with IL-22-receptor mimetics and IL-22 receptors. This procedure determines potential ligands or mimetics of a IL-22. The actual IL-22-ligand complexes

or mimetics are crystallized and analyzed using X-ray diffraction. The diffraction pattern coordinates are similarly used to calculate the three-dimensional interaction of a ligand and the IL-22.

An amino acid sequence of a IL-22 protein and/or X-ray diffraction data, useful for computer molecular modeling of IL-22, can be "provided" in a variety of mediums to facilitate use thereof. As used herein, provided refers to a manufacture, which contains, for example, a IL-22 amino acid sequence and/or atomic coordinate/X-ray diffraction data of the present invention, e.g., an amino acid sequence of SEQ ID NO: 2, a representative fragment thereof, or an amino acid sequence having at least 80-100% overall identity to an amino acid sequence of SEQ ID NO: 2. Such a method provides the amino acid sequence and/or X-ray diffraction data in a form which allows a skilled artisan to analyze and molecular model the three-dimensional structure of a IL-22-related protein, including one or more subdomains thereof.

In one application of this embodiment, IL-22, or at least one subdomain thereof, amino acid sequence and/or X-ray diffraction data of the present invention is recorded on computer readable medium. As used herein, "computer readable medium" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as optical discs or CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon an amino acid sequence and/or X-ray diffraction data of the present invention.

As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any known method for recording information on computer readable medium to generate manufactures comprising an amino acid sequence and/or atomic coordinate/X-ray diffraction data information of the present invention. A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon an

amino acid sequence and/or atomic coordinate/X-ray diffraction data of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the sequence and X-ray data information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and MICROSOFT Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of dataprocessor structuring formats (e.g. text file or database) in order to obtain computer readable medium having recorded thereon the information of the present invention.

By providing computer readable medium having stored thereon an IL-22 or related sequence protein and/or atomic coordinates based on X-ray diffraction data, a skilled artisan can routinely access the sequence and atomic coordinate or X-ray diffraction data to model a IL-22 or related protein, a subdomain thereof, mimetic, or a ligand thereof. Computer algorithms are publicly and commercially available which allow a skilled artisan to access this data provided in a computer readable medium and analyze it for molecular modeling and/or RDD. *See, e.g.,* Biotechnology Software Directory, MaryAnn Liebert Publ., New York (1995). A variety of comparing means can be used to compare a target sequence or target motif with the data storage means to identify structural motifs or electron density maps derived in part from the atomic coordinate/X-ray diffraction data. A skilled artisan can readily recognize that any one of the publicly available computer modeling programs can be used as the search means for the computer-based systems of the present invention.

Several approaches can be taken for the use of the crystal structure of a IL-22 in the rational design of a relevant activity similar to that of the unmutated IL-22. A computer-assisted, manual examination of an IL-22-receptor-binding site structure is optionally done. Software such as GRID (Goodford (1985) *J. Med. Chem.* **28:** 849-857), a program that determines probable interaction sites between probes with various functional group characteristics and the protein surface, is used to analyze the surface sites to determine structures of similar inhibiting proteins or compounds. The GRID

calculations, with suitable inhibiting groups on molecules (*e.g.,* protonated primary amines) as the probe, are used to identify potential hotspots around accessible positions at suitable energy contour levels.

A therapeutic IL-22 or related protein of the present invention can be, but is not limited to, IL-22-receptor ligands that bind to IL-22 receptors as either agonists or antagonists; IL-22-receptor-chain mimetics or antibodies that bind to endogenous IL-22 and impairs the binding of IL-22 to endogenous receptors. The program DOCK (Kuntz *et al.* (1982) *J. Mol. Biol.***161:** 269-288) may be used to analyze receptor binding sites, dimerization interfaces and/or ligand binding site and suggest ligands or amino acid residues with complementary steric properties. Several methodologies for searching three-dimensional databases to test pharmacophore hypotheses and select compounds for screening are available. These include the program CAVEAT (Bacon *et al.* (1992) *J. Mol. Biol.* **225:** 849-858), which uses databases of cyclic compounds which can act as "spacers" to connect any number of chemical fragments already positioned in the active site. This allows one skilled in the art to quickly generate hundreds of possible ways to connect the fragments already known or suspected to be necessary for tight binding. The program LUDI (Bohm *et al.* (1992) *J. Comput.-Aid. Mol. Des.* **6:** 61-78) can determine a list of interactions sites into which to place both hydrogen bonding and hydrophobic fragments. LUDI then uses a library of approximately 600 linkers to connect up to four different interaction sites into fragments. Then smaller "bridging" groups such as --CH2-- and --COO-- are used to connect these fragments. For example, for the enzyme DHFR, the placements of key functional groups in the well-known inhibitor methotrexate were reproduced by LUDI. *See also,* Rothstein *et al.* (1992) *J. Med. Chem.* **36:** 1700-1710.

Once IL-22-receptor ligands or mimetics are identified, crystallographic studies of, the IL-22 ligand and its receptor complex and the IL-22-receptor mimetic and its IL-22 complex may be performed to confirm and refine the ligand or mimetic properties. Direct measurements of receptor binding or complex formation provide further confirmation that the modeled mimetic and ligands are high affinity IL-22 agonists, antagonists or inhibitors. Any suitable assay for receptor binding or complex formation may be used. The atomic coordinates of IL-22 are useful in the generation of molecular models of related proteins and of IL-22-receptor mimetics and ligands. Utilizing

CLUSTAL (a multiple sequence alignment program in PC-Gene) and the Homology module (a structure-based homology modeling program in InsightII on a Silicon Graphics Incorporated workstation), molecular models (and the corresponding three-dimensional coordinates files) of numerous mimetics and ligands are generated. With these files, mutants and mimetics of the present invention are mapped and new ones designed. The results described herein demonstrate that tight-binding mimetics and ligands of an IL-22 receptor, or related protein, based on the crystal structure of IL-22, are provided by the present invention.

The term "antibody" as used herein, unless indicated otherwise, is used broadly to refer to both antibody molecules and a variety of antibody-derived molecules. Such antibody-derived molecules comprise at least one variable region (either a heavy chain of light chain variable region) and include molecules such as Fab fragments, $F(ab)_2$ fragments, single chain (sc) antibodies, diabodies, triabodies, tetrabodies, individual antibody light chains, individual antibody heavy chains, chimeric fusions between antibody chains and other molecules, and the like. As used herein "antigen-binding fragment" or "antigen-binding domain" or "Fab fragment" refer to the about 45 kDa fragment obtained by papain digestion of an immunoglobulin molecule and consist of one intact light chain linked by disulfide bond to the n-terminal portion of the contiguous heavy chain. As used herein, "$F(ab)_2$ fragment refers to the about 90 kDa protein produced by pepsin hydrolysis of an immunoglobulin molecule. It consists of the N-terminal pepsin cleavage product and contains both antigen binding fragments of a divalent immunoglobulin, such as IgD, IgE, and IgG. Neither the "antigen-binding fragment" nor "$F(ab)_2$ fragment" contain the about 50 kDa F_c fragment produced by papain digestion of an immunoglobulin molecule that contains the c-terminal halves of the immunoglobulin heavy chains, which are linked by two disulfide bonds, and contain sites necessary for compliment fixation.

As used herein, the term "humanized" antibody refers to a molecule that has its CDRs—complementarily determining regions—derived from a non-human-species immunoglobulin and the remainder of the antibody molecule derived mainly from a human immunoglobulin. As used herein "immunoglobulin" refers to any member of a group of glycoproteins occurring in higher mammals that are major components of the

immune system. As used herein, "immunoglobulins" comprise four polypeptide chains-2 identical light chains and two identical heavy chains that are linked together by disulfide bonds. An immunoglobulin consists of the antigen binding domains, which are each comprised of the light chains and the end-terminal portion of the heavy chain, and the F_c region, which is necessary for a variety of functions, such as compliment fixation. There are five classes of immunoglobulins wherein the primary structure of the heavy chain, in the F_c region, determines the immunoglobulin class. Specifically, the alpha, delta, epsilon, gamma, and mu chains correspond to IgA, IgD, IgE, IgG and IgM, respectively. As used herein "immunoglobulin" includes all subclasses of alpha, delta, epsilon, gamma, and mu and also refers to any natural (*e.g.*, IgA and IgM) or synthetic multimers of the four-chain immunoglobulin structure.

As used herein, "Fv or Fv fragment" refers to the N-terminal part of the Fab fragment of an immunoglobulin molecule, consisting of the variable region of the heavy chain and the variable region of the light chain. As used herein, "scFv" refers to a polypeptide comprising the heavy chain variable region and light chain variable region of a parent immunoglobulin, wherein the heavy chain variable region and the light chain variable region are linked by a peptide linker. As used herein, "diabody" refers to an scFv dimer. As used herein, "triabody" refers to an scFv trimer, and "tetrabody" refers to an scFV tetramer. As used herein, "heavy chain" refers to the heavier of the two types of polypeptide chain in immunoglobulin molecules that contain the antigenic determinants that differentiate the various Ig classes, *e.g.*, IgA, IgD, IgE, IgG, IgM, and the domains necessary for compliment fixation placental transfer, mucosal secretion, and interaction with F_c receptor. As used herein, "heavy chain variable region" refers to the amino-terminal domain of heavy chain that is involved in antigen binding and combines with the light chain variable region to form the antigen binding domain of the immunoglobulin. As used herein, "light chain" refers to the shorter of the two types of polypeptide chain in an Ig molecule of any class. Light chains comprise variable and constant regions. As used herein, "light chain variable region" refers to the amino-terminal domain of the light chain and is involved in antigen binding and combines with the heavy chain to form the antigen binding region.

The term "variable region" as used herein in reference to immunoglobulin molecules has the ordinary meaning given to the term by the person of ordinary skill in the art of immunology. Both antibody heavy chains and antibody light chains may be divided into a "variable region" and a "constant region." The point of division between a variable region and a constant region may readily be determined by the person of ordinary skill in the art by reference to standard texts describing antibody structure, *e.g.* Kabat *et al.* (1991) Sequences of Proteins of Immunological Interest. 5th Edition. U.S. Department of Health and Human Services, U.S. Government Printing Office.

The recombinant production of immunoglobulin molecules, including humanized antibodies are described in U.S. Pat. No. 4,816,397 (Boss *et al.*), U.S. Pat. No. 4,816,567 (Cabilly *et al.*) U.K. patent GB 2,188,638 (Winter *et al.*), and U.K. patent GB 2,209,757; all of which are incorporated herein by reference. Techniques for the recombinant expression of immunoglobulins, including humanized immunoglobulins, can also be found, among other places in Goeddel *et al.* (1991) Gene Expression Technology, *Methods in Enzymology* Vol. 185, and Borreback (1992) Antibody Engineering, W. H. Freeman, all of which are incorporated herein by reference. Additional information concerning the generation, design and expression of recombinant antibodies can be found in Mayforth (1993) Designing Antibodies, Academic Press, San Diego and Harlow (1988) Antibodies—A laboratory manual. First Edition. Cold Spring Harbor Laboratory, all of which are incorporated herein by reference.

Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the compounds of the present invention and practice the claimed methods. The following working examples therefore, specifically point out preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

EXAMPLES

Example 1: Protein expression and purification.

A cDNA encoding IL-22 sequence lacking the signal peptide was subcloned into the *E. coli* expression vector pET2a, generating pEThTIF. The recombinant protein expressed from this vector contains a methionine at the N-terminus, followed by the amino acid sequence starting at Gln29 to the C-terminus. Vector pEThTIF was transformed into *E. coli* strain BL21 (DE3)-codon plus-RII. The resulting strain was maintained in LB medium containing Ampicillin (100 μg/ml) and Chloramphenicol (34 μg/ml). Induction of IL-22 express was performed at 37°C for 4 hours with 1 mM IPTG, which was added when the cultures reached an OD_{660} of approximately 1.0-1.3. Under these conditions, up to 50 mg/1 of IL-22 were obtained. Cells were lysed by using a high pressure cell (French Press) and the inclusion bodies were washed once in buffer containing 50 mM Tris-HC1, pH 8.0, 100 mM NaCl, 1 mM EDTA, 1 mM DTT and 0.5% sodium deoxycholate and once in the same buffer lacking sodium deoxycholate. The inclusion bodies were solubilized in 25 mM MES pH 5.5, 8 M urea, 10 mM EDTA, and 0.1 mM DTT. Protein concentration was adjusted to 100 μg/ml and refolded by dialysis in buffer containing Tris-HC1 pH 8.0, 0.5 M arginine, 1 mM reduced glutathione, 0.1 mM oxidized glutathione, 2 mM EDTA and 0.1 mM PMSF. Refolding was performed for 20 h at 4°C. Refolded samples were concentrated 100 fold with a YM3 AMICON membrane and loaded onto a Superdex 75 10/30 HP column (Amersham-Pharmacia), which was eluted with buffer containing 25 mM MES pH 5.4 and 150 mM NaCl. Human IL-22 peak fractions were concentrated to 5 mg/ml with a YM3 AMICON membrane and desalted using a Hiprep 26/10 column (Amersham-Pharmacia) with elution buffer containing 10 mM MES pH 5.4. Human IL-22 was concentrated again to 5 mg/ml and lyophilized in 1 mg fractions.

Example 2: Protein crystallization.

Preliminary screening of the crystallization conditions was performed using a sparse-matrix screen at 291 K (Crystal Screen I and II, Hampton Research Corp.). Small

crystals were found in the condition number 18, 26 and 29 of the Crystal Screen I kit. Several attempts to enhance crystal quality were performed, including pH and precipitant concentration refinement, detergent addition, and macroseeding. Well diffracting crystals were obtained in hanging drops equilibrated against a reservoir solution consisting of 0.9 M sodium tartrate, TRITON X-100 detergent and 0.1 M HEPES at pH 7.5. The crystallization drops contained equal volumes (1µl) of reservoir and purified IL-22 (10 mg/ml in 20 mM MES buffer at pH 5.4) solutions. The protein crystallized in the space group $P2_12_12_1$, with unit-cell dimensions a=55.43, b=61.61, c=73.43 Å.

Example 3: Data collection.

Crystals were soaked in different cryosoaking solutions, mounted in a rayon loop and finally flash-cooled to 80°K in a cold-nitrogen stream. Data collection was performed at the Protein Crystallography beamline (LNLS, Campinas, Brazil; Dumoutier *et al.* (2000) *Genes and Immunity* **1:** 488-494; Cookson, (2000) *Nature* **402s:** B5-B11) and at the X4A beamline (NSLS, Upton, USA), using a MAR345 image plate and a Quantum-4 CCD detector, respectively. Three diffraction datasets were collected to a resolution beyond 1.95 Å. Diffraction images were processed and scaled with the programs DENZO and SCALEPACK. *See e.g.,* Walter *et al.* (1995) *Biochemistry* **34:** 12118-12125.

Example 4: Heavy-atom derivatives and phasing.

The structure was solved by SIRAS. An iodine derivative was obtained by soaking the crystal for 180 seconds in 2µl of cryoprotectant solution containing 0.125 M sodium iodide following the novel "quick cryo soaking" derivatization procedure. *See e.g.,* Kotenko *et al.* (1997) *EMBO J.* **16**: 5894-5903; Zdanov *et al.* (1995) *Structure* **3:** 591-601. The data sets of an iodine derivative (I-IL-22) and a native crystal (Nat-IL-22) were collected at the Protein Crystallography beamline (Dumoutier *et al.* (2000) *Genes and Immunity* **1:** 488-494; Cookson (2000) *Nature* **402s:** B5-B11) at LNLS (Campinas, São Paulo, Brazil). The heavy-atom positions of the iodine derivative were determined by direct methods with the programs DREAR (Ealick *et al.* (1991) *Science* **252:** 698-

702) and SnB 2.1 (Josephson *et al.* (2000) *J. Biol. Chem.* **275:** 13552-13557). The bimodal distribution of the R_{min} histogram was used to identify the correct solution (Trèze (1999) The cytokine network and immune functions. Oxford University Press, Oxford; Barton, (1993) *Protein Eng.* **6:** 37-40). The heavy-atom substructure obtained directly from SnB was initially refined with the CNS package using anomalous and isomorphous difference Fourier maps. Refined coordinates were then input into SHARP (Otwinowski *et al.* (1997) *Methods Enzymol.* **276:** 307-326) for phase calculation, resulting in an overall figure of merit of 0.45 for all reflections in the range of 21.7 – 2.40 Å. Density modification with solvent flattening was performed using the program SOLOMON. *See e.g.,* Blessing, *et al.* (1999) *J. Appl. Cryst.* **32:** 664-670. Due to the high resolution and completeness of the I-IL-22 data set, and also the quality of solvent-flattened electron-density map, an automatic construction of an IL-22-hybrid model could be performed by the ARP/wARP program. *See e.g.,* Thiel, *et al.* (2000) *Structure* **8:** 927-936. The nucleotide-based IL-22 primary structure was used in the final-model-side-chain assignment. *See e.g.,* Dumoutier *et al.* (2000) *Proc. Natl. Acad. Sci. U.S.A.* **97:** 10144-10149.

One mercury derivative was also obtained using traditional methods of derivatization. The Hg derivative (Hg-IL-22) data set was collected at the X4A beamline at NSLS (Upton, New York, USA) and was used at latter stages of refinement and construction of disordered loops. This latter derivative was prepared using traditional methods for derivatization of protein crystals. Details of native and derivative crystal preparation, as well as data statistics, are summarized in Table 1.

Example 5: Model building.

1. Refinement.

A. The initial model was obtained without manual intervention after 6 ARP/wARP jobs and more than 4000 REFMAC cycles. *See e.g.,* Weeks, *et al.* (1999) *J. Appl. Cryst.* **32:** 120-124. In the last cycle, after almost 72 hours of uninterrupted CPU time in a Pentium III 500 MHz, 81.6% of the total amino acid residues were corrected traced.

B. The initial structure of IL-22 was improved by a number of cycles of refinement and rebuilding using CNS package. *See e.g.,* Polikarpov, *et al.* (1997) *J. Synchrotron Rad.* **5:** 72-76. Interlaced refinement of model against Nat-IL-22, Hg-IL-22 and I-IL-22 data sets were used to allow a complete trace of main chain atoms through disordered regions. The initial model contained 231 amino acid residues (in nine distinct chains) and 809 water molecules. The isolated cDNA of IL-22 encodes a protein of 179 amino acids, of which the first 22 amino acids are predicted to function as a signal sequence. (Xie *et al.* (2000) *J. Biol. Chem.* **275:** 31335-31339). The N-terminal amino acid analysis of IL-22 confirms that the mature protein begins at amino acid residue 34. Construction of disordered loops and filling of main chain gaps were performed manually using the program O. *See e.g.*, Debaerdemaeker, *et al.* (1983) *Acta Cryst.* A**39:** 193-196. Finally, the model was refined against a Nat-IL-22 data set, starting with a simulated annealing protocol in the program CNS. After several iterations of energy minimization, B-factor refinement, and bulk-solvent and anisotropic corrections, the final R_{factor} and R_{free} were 0.191 and 0.225, respectively, for the Nat-IL-22 data in the resolution range of 21.7 – 1.92 Å. The final model includes 283 residues (two chains) and 189 water molecules. The refined model of IL-22,a dimer in the asymmetric unit (Fig. 1a), includes monomer A with 142 amino acid residues (Ser38-Ile179), monomer B with 141 amino acid residues (His39-Ile179) and 189 water molecules. About 93.8% and 6.2% of the amino acid residues adopt a conformation that corresponds to the most favored and additionally allowed regions of the Ramachandran plot, respectively. *See e.g.*, Table 2 for further information about refinement and geometry statistics. No residues have been encountered in the disallowed regions of the Ramachandran plot.

As shown in Figure 1b, each monomer of IL-22 model is characterized by six α-helices (A-F) that fold in a compact bundle. Helix A (amino acid residues Lys44-Ser64) is linked to a short helix B (Glu77-Pe80) by a large loop AB (Leu65-Gly76). Helix A has a kink at Gln48-Gln49, presumably due to a hydrogen bond between Nϵ-Gln49 and O-Ser45 (2.79 Å and 2.55 Å in monomers A and B, respectively). This divides helix A into unequal parts: A_1 and A_2. The loop BC (His81-Glu87) connects helix B to helix C (Arg88-Glu102). The helix C is joined to helix F by a disulfide bond between Cys89 and Cys178. Another loop (CD; Val103-Try114) links helix C to helix D (Met115-Leu129).

According to PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26:** 283-291), a small difference in secondary structure between monomers is observed at the loop CD region. A small α-helix is observed between amino acid residues Phe105 and Gln107 of the monomer B. Helix D is connected to helix E by a disordered loop (DE; Ser130-Asp138). This loop is stabilized, at least in the vicinity of Cys132, by another disulfide bond between Cys132 and Cys40, the latter in the N-terminal coil. Finally, a simple junction EF (Gly156) joins the last two helices E (Leu139-Leu155) and F (Glu157-Cys178). Probably, as a consequence of a disulfide bond between Cys89 and Cys178, the latter belonging to the C-terminal of helix F, a kink at Glu166 divides helix F into two parts: F_1 and F_2.

2. Dimer formation.

An expressive part (61%) of the volume of the asymmetric unit (6.27×10^4 Å^3) is occupied by a dimer of IL-22. A small fraction of this volume (8%) is filled with ordered water molecules. The monomers are essentially equal, however, a number of significant differences in the main chain conformation are observed in the vicinity of amino acid residues Gln48, Asn69, Gln136 and Lys154 (Fig. 2). These differences are mostly explained by crystallographic and non-crystallographic contacts. The reason for a significant positional difference between monomers around Gln48 is the fact that this region in monomer A is involved in interface interactions, whereas the same region in monomer B is exposed to the solvent. In addition, the presence of two intramolecular interactions—Oδ1-Asp43/Oγ-Ser45 with 2.64 Å in monomer A and O-Asn46/Nε2-Gln49 with 2.55 Å in monomer B—contribute to a relative change in main-chain atoms positions between residues Leu42 and Pro50. A second conformational difference around Asn69 is a consequence of a crystallographic contact between side chain atoms of Asn69 and Thr70 of monomers A and B, respectively. Gly136 is localized in the disordered loop DE. This fact explains the root-mean-square-deviation (rmsd) around 2.0 Å in the vicinity of this amino acid residue. Finally, the last major difference between monomers is found close to Lys154. In this region, three distinct interactions of Lys153 and Lys154 from monomer B—Oε1-Glu102/Nζ-Lys153 with 2.68 Å, Oδ1-Asn46/Nζ-Lys153 with 2.78 Å and Oε1-Glu160/Nζ-Lys154 with 2.80 Å, which are absent in monomer A—are responsible for a high rmsd of main-chain atoms.

Unlike the hIL-10, the IL-22 dimeric structure formation does not require the intertwining of the main chain of each monomer (Fig. 1). An interface area of approximately 2250 Å^2, which corresponds to 30% of the total surface area of a monomer, is involved in the dimer formation. The buried surface for the chosen dimer conformation is at least two times larger than any other buried surface area (~ 960 Å^2 or less). Also, the dimer interface, which is formed mostly by residuesArg41 to Phe80 and Asp168 to Ile179 in monomer A and Thr53 to Arg88 and Glu166 to Ile179 in monomer B, has a significant number of hydrophobic residues. Intermolecular interface contacts closer than 3.2 Å are listed in Table 3. The electrostatic and hydrophobic distribution of the IL-22 surface together with the position of the principal amino acid residues involved in the formation of the dimer are given in Fig. 3.

According to the predicted primary structure, human IL-22 has three potential glycosylation sties (Asn-Xaa-Thr/Ser) localized in helix A (Asn54-Arg55-Thr56) (site #1), loop AB (Asn68-Asn69-Thr70) (site #2) and helix C (Asn97-Phe98-Thr99) (site #3). Since the recombinant IL-22 used in crystallization is not glycosylated, we attempted the analysis of the possible interactions between oligosaccharides and IL-22 by calculating the accessible area of each residue in all three putative glycosylation sites. The results demonstrate that site #2, localized at the loop AB, is the one with the larger accessible area. A solvent-accessible area of approximately 37 Å^2 was found for Nδ2-Asn68 and for Oγ1-Thr70 atoms, indicating that there is no steric hindrance to their participation in N-glycosyl and O-glycosyl links, respectively. On the other hand, sites #1 and #3 seem to participate only in N-glycosyl linkages. The accessible area of Oγ1-Thr56 and Oγ1-Thr99 is 0 and 6 Å^2, whereas Nδ2-Asn54 and Nδ2-Asn97 atoms possess, respectively, the surface-accessible area of 24 and 18 Å^2. This structural analysis is in agreement with biochemical studies suggesting that these three sites are of N-glycosyl type. (Kotenko *et al.* (2001) *J. Biol. Chem.* **276:** 2725-2732). Consistent with biophysical observations, the present structure shows that putative glycosylation sites #1 and #2 reside near the dimer interface, and that glycosylation at these positions would disrupt dimer formation.

3. Comparison of IL-22 to the structures of IL-10 and IFN-γ.

As shown in Figure 2, the crystallographic structure of hIL-22 is a compact dimer, with a buried surface area of approximately 2250 Å^2. Several intermolecular interactions along the interface surface keep the monomers together. Each monomer is formed by six α-helices (A-F) from the same polypeptide chain. Quite in contrast, the crystallographic structures of hIL-10 (Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103:** S485-S491; Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26:** 283-291; Kraulis *et al.* (1991) *J. appl. Cryst.* **24:** 946-950) and hIFN-γ (Esnouf (1997) *J. Mol. Graph.* **15:** 133-138; McLane *et al.* (1998) *Am. J. respir. Cell Mol. Biol.* **19:** 713-720) revealed the presence of a homodimer composed of two α-helical domains formed by intertwining of α-helices donated by the first and the second monomer composing a dimer. The first four helices of one chain (A-D), together with the helices E' and F' from the second chain, compose the first domain. Helices A' to D', E and F form the second domain.

There are significant structural similarities between IL-22, IL-10 and IFN-γ (Fig. 4). In all these proteins, helices A to D of each monomer form a rigid frame with a highly hydrophobic depression in its middle. This depression is covered in IL-22 by helices E and F from the same monomer, whereas in hIL-10 and hIFN-γ this is accomplished by helices E' and F' (from the second monomer). The basic reason for these differences is in the loop DE. There are two cysteine residues Cys126 and Cys132 at the hIL-10 DE loop that make two distinct disulfide bonds with residues Cys30 and Cys80, respectively. (Here we adopted the residue numbering according to the hIL-10 cDNA sequence). These two S-S bridges restrict the flexibility of the amino acid chain and the length of the loop DE in such a manner that helices E and F can not fold onto their respective monomer to occupy position of their counterparts E' and F'. This leads to the intertwined dimer formation. *See e.g.*, Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103:** S485-S491; Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26:** 283-291; Kraulis *et al.* (1991) *J. appl. Cryst.* **24:** 946-950. A monomeric form of hIL-10 could only possibly be created when the Cys80-Cys132 disulfide bond were to be reduced, or if a small amino acid chain were inserted after Cys132. *See e.g.*, Levitt *et al.* (1999) *J. Allergy Clin. Immunol.* **103:** S485-S491. The latter approach has been applied with success to hIL-10, where insertion of a small polypeptide linker in the loop that connects

the swapped secondary structure elements led to the formation of a monomeric protein. *See e.g.*, Merritt, *et al.* (1997) *Methods Enzymol.* **277:** 505-524. Similarly, the hIFN-γ intertwined dimer is formed because the loop DE is not long enough to allow the fold of helix E and F into the same domain.

In IL-22, just one disulfide bond (Cys40-Cys132) exists at the loop DE, which allows sufficient flexibility and extension of the loop to bring helices E and F into close contact with helices A to D and to complete the folding of the monomer. A second disulfide bond, in the C-terminal of helix F (Cys89-Cys178), adds to a rigidity of a final IL-22 structure.

The best superposition of IL-22 onto hIL-10 and hIFN-γ was obtained using a single domain of the hIL-10 and hIFN-γ onto IL-22 yielding an rmsd of 1.9 Å and 2.3 Å for 432 and 300 pairs of main chain atoms, respectively. Helices A to D of the IL-22 monomer superimpose with helices A to D of one of the monomers of hIL-10 and hIFN-γ. Helices E and F fit nicely into the spatial position occupied by helices E' and F' of the second monomer. The three-dimensional superposition of the structures allowed us to perform a structure-based sequence alignment for IL-22 and IL-10 that is shown in Figure 5. Inspection of the superposition of IL-22 and hIL-10 revealed strong similarities in the conformation of the main-chain trace of helices E (E') and F (F'), and to a lesser extent, the conformation of several parts of loop AB, helix C and helix D. Each of these regions represent high sequence similarity. Some significant differences in the regions of the N-terminal coil, helix A, helix B, loop BC, loop CD and loop DE were also observed.

Reasonable superposition of hIL-10 or hIFN-γ dimers onto IL-22 dimer was proven to be impossible. In each case, dimer formation is so much different that only one domain of IL-22 could be superimposed with an hIL-10 (or hIFN-γ) domain. A second domain of each structure occupies completely different spatial positions (Figs. 4c and 4d). Whereas the intertwining of α-helices is essential for the formation and integrity of molecules adapting a form of the V-shaped dimers (*i.e.*, hIL-10 and hIFN-γ), in IL-22 dimer formation is not required for folding. It must be stressed that the buried

surface on the hIL-2 interface coincides with the outer part of the hIL-10 and hIFN-γ V-shaped-dimer surfaces (Figs. 4c and 4d).

4. Receptor binding sites.

Two receptor chains—CRF2-4 and CRF2-9—have been identified for IL-22. The CRD2-4 receptor chain is common between IL-22 and IL-10 and is necessary for signaling, whereas CRD2-9 is specific for IL-22. *See e.g.*, Xie *et al.* (2000) *J. Biol. Chem.* **275:** 31335-31339; Kotenko *et al.* (2001) *J. Biol. Chem.* **276:** 2725-2732; both incorporated herein by reference. CRF2-9 bears primary sequence homology to the another receptor chain of IL-10—IL-10R1. The binding affinity of IL-22 and IL-10 to CRF2-4 is different. CRF2-4 alone is sufficient to bind IL-22, while the presence of a second receptor chain is required for efficient IL-10 binding. Moreover, both CRF2-9 and CRF2-4 share significant sequence homology to the IFN-γ receptor, IFN-γRα. The three-dimensional structure of hIFN-γRα was recently solved as a complex with its ligand (McLane *et al.* (1998) *Am. J. Respir. Cell Mol. Biol.* **19:** 713-720; incorporated herein by reference), and the structure of IL-22 was superimposed onto the structure of the hIFN-γ/hIFNRα complex to identify the residues involved in IL-22/receptor interactions. A similar structural comparison with the hGH/hGHBP complex has been used in receptor-binding-site analysis of IL-10. *See e.g.*, Levitt, *et al.* (1999) *J. Allergy Clin. Immunol.* **103:** S485-S491; incorporated herein by reference.

The superposition of IL-22 onto the hIFN-γ/hIFNRα complex indicates that one possible receptor binding site is localized in the region formed by helix A, loop AB and helix F of IL-22 (Region 1, R1; see Figures 4d and 6a). Among the 17 residues involved in hIFN-γ/hIFNRα interactions (closer than 3.4 Å), only two residues do not have their IL-22 structural counterparts localized in R1. Nine of the seventeen residues localized in R1 are not sufficiently close to their hIFN-γ counterparts, which may explain the inability of IL-22 to bind to hIFN-γRα. The major differences between hIFN-γ and IL-22 within R1 are observed in the loop AB and distances of more than 7 Å are found between their main chains. As shown in Figure 6b, six relatively conserved residues (Lys61, Thr70, Asp71, Lys162, Glu166 and Leu169), however, occupy almost the same spatial position as six hIFN-γ residues—Lys35, Asp47, Asn48, Lys131, Glu135, Gln138.

A comparison with the hIL-10 putative receptor binding site (Levitt, *et al.* (1999) *J. Allergy Clin. Immunol.* **103:** S485-S491; incorporated herein by reference) shows that Region 1—helix A, loop AB and helix F' in the case of hIL-10—is involved in receptor interactions. Amino acid residues Gln60, Asp62, Asn63, Lys156, Glu160, Asp162, Asp166 and Glu169 of the hIL-10 binding site having their IL-22 counterparts in residues Asn68, Thr70, Asp71, Lys162, Glu166, Asp168, Met172 and Arg175. Among these eight residues, Thr70, Asp71, Lys162 and Glu166 were also found in the IL-22:IFN-γ/INF-γRα comparison. The superposition of the hIL-10 putative binding Region 1 onto IL-22 is shown in Figure 6c. The three-dimensional structure comparison of IL-22 with either IFN-γ/INF-γRα or hGH/hGHBP complexes demonstrates that Region 1 is the receptor binding site.

The three-dimensional similarities observed between IL-22 and hIL-10 in Region 1, especially between helices F and F', also indicate that this region is the CRF2-4 binding site. In addition, the gylcosylation site in the IL-22 AB loop may interfere with receptor binding. The homology of INF-γRα CRF2-9 also suggests that R1 is the recognition/binding site for CRF2-9. Notably, in the present crystallographic model, the region 1 of each monomer is hidden at the dimer interface. Moreover, a few potential receptor-binding residues are directly involved in dimer formation (see Table 3). Therefore, a IL-22-receptor chain can only bind a monomer of IL-22, and thus, requires the dissociation of the dimer observed in the present crystallographic structure. In contrast, the hIL-10 dimer does not require disruption prior to interaction with the receptor, since the hIL-10-receptor-binding site is localized at the outer part of the B-shaped-dimer surface (Figures 4c and 4d).

Although the RZ binding site in IL-22 cannot be easily inferred from inspection of the interactions between hINF-γ and hINF-γRα, region Z, which comprises the terminal portions of helices C and E of each IL-22 monomer, is a binding site for CRF2-4. A sequence comparison between IL-22 and several IL-10 identifies several amino acids that are conserved within the Region 2 (R2) region—FTLEEVL (SEQ ID NO: 4) and KLGE (SEQ ID NO: 5) in IL-22 helices C and E, respectively. Region 2 is localized at the surface of IL-22, which is opposite to R1. Localization of each binding region (R1 and R2) on the opposite sides of the IL-22 molecule allows IL-22 to interact

with two receptor chains simultaneously. In hIL-10, the amino acids corresponding to the region R2 are localized at the inner part of the V-shaped dimer surface. The angle between each hIL-10 domain in the V-shaped dimer is large enough to allow interaction of two CRF2-4 receptor chains with the two binding sites in RZ 2 (Figure 4c).

Table 1. Details of the preparation and data-collection statistics of IL-22 crystals. Statistical values for the highest resolution shells are shown in parentheses.

	Nat-IL-22	I-IL-22	Hg-IL-22
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Unit cell parameters (Å)	a=55.43; b=61.61;	a=56.05; b=61.78;	
a=56.04;b=61.71;			
	c=73.47	c=73.63	c=74.61
Resolution (Å)	21.7 - 1.92	21.8 - 1.92	22.4 - 1.90
	(1.96 - 1.92)	(1.96 - 1.92)	(1.97 - 1.90)
No. of reflections	67677	182876	55855
No. of unique reflections[1]	18139	37777	29854
$\langle I/\sigma(I)\rangle$	14.4 (2.5)	13.4 (3.1)	8.2 (2.1)
Multiplicity	3.7 (3.1)	4.8 (4.3)	1.9 (1.7)
Completeness	91.2 (75.1)	99.9 (99.7)	75.9 (77.9)
R_{merge}[2]	8.6 (50.8)	11.7 (43.9)	10.0 (49.9)
Data collected (degrees)	103.2	248.6	70.0
Cryoprotectant solution	Mother liquor	Mother liquor	Mother liquor
	15% ethyl. glycol	15% ethyl. glycol	15% ethyl.
glycol			
		0.125 M NaI	5 mM $HgCl_2$
Soaking time	30 seconds	180 seconds	10 hours

[1] Multiplicity of derivative (native) data sets calculated with Friedel-related reflections treated separately (as equivalent).

[2] $R_{merge} = \Sigma hkl \; |I_{hkl} - \langle I_{hkl}\rangle| \; / \; \Sigma_{hkl} \; I_{hkl}$

Table 2. Refinement statistics and quality of the IL-22 model.[1]

GENERAL INFORMATION	
Disulfide bonds	Cys40-Cys132 and Cys89-Cys178
Cis-peptides	Pro113
Alternative conformations	Met172 in monomer A
	Asp43, Ser45, Arg55, Ile75, His81,
	Arg124, Ile161 and Leu174 in monomer B
REFINEMENT STATISTICS (21.7 – 1.92 Å)	
Total number of reflections	17238
Working set number of reflections	16372
R-factor (%)	19.1
Test set number of reflections	866
R-free (%)	22.5
Total number of protein atoms	2330
Total number of water molecules	189
GEOMETRY STATISTICS	
Rmsd bond distances (Å)	0.006
Rmsd bond angles (°)	1.1
Average B factors	
residue atoms (Å^2) (A, B)	24.3 (22.3, 26.2)
mainchain atoms (Å^2) (A, B)	22.1 (20.2, 24.1)
sidechain atoms (Å^2) (A, B)	26.3 (24.4, 28.1)
water molecules (Å^2)	37.3
Average rmsd B factor	
residue atoms (Å^2) (A, B)	2.5 (2.6, 2.5)
mainchain atoms (Å^2) (A, B)	1.0 (1.0, 1.0)
sidechain atoms (Å^2) (A, B)	1.9 (2.0, 1.8)
water molecules (Å^2)	11.4
Ramachandran plot [2]	
residues in most favored region (%)	93.8
residues in additionally allowed regions (%)	6.2
residues in generously allowed regions (%)	0.0
residues in disallowed regions (%)	0.0

Table 2. Continued[1]

NON-CRYSTALLOGRAPHIC SYMMETRY [3]	
Rmsd coordinates	
Cα atoms (Å)	0.911
mainchain atoms (Å)	0.884
all bonded atoms (Å)	1.670
Rmsd B factors	
Cα atoms (Å^2)	10.04
mainchain atoms (Å^2)	10.05
all bonded atoms (Å)	10.77

[1] Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

[2] Residue regions as defined by PROCHECK (Laskowski *et al.* (1993) *J. Appl. Crystallogr.* **26:** 283-291).

[3] Non-crystallographic symmetry of subunits A and B.

Table 3. Intermolecular contacts (monomers A* and B**). The distance cut-off of 3.2 Å was used.[1]

Residue*	Atom*	Residue**	Atom**	Distance (Å)
Arg175	Nη2	Glu166	Oε1	2.57
Phe57	O	Asn176	Nδ2	2.64
Arg73	Nη2	Val83	O	2.71
Lys44	Nζ	Ser64	Oγ	2.85
Arg175	Nη1	Asp168	Oδ2	2.86
Asn176	Nδ2	Ile75	O	2.91
Gln48	O	Lys61	Cε	2.96
Lys44	Nζ	Glu166	Oε1	2.98
Lys61	Nζ	Ile179	OT1	3.12
Gln49	Oε1	Lys61	Nζ	3.15

[1] Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

[1] Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

Table 4. Atomic Coordinates of human IL-22 determined as described herein.[1]

CRYST1	55.430	61.610	73.470	90.00	90.00	90.00	P 21 21 21
SCALE1	0.01804	0.00000	0.00000	0.00000			
SCALE2	0.00000	0.01623	0.00000	0.00000			
SCALE3	0.00000	0.00000	0.01361	0.00000			

ATOM	1	CB	SER	A	38	8.633	14.375	24.449	1.00	47.79	A	C
ATOM	2	OG	SER	A	38	8.362	14.381	23.062	1.00	49.55	A	O
ATOM	3	C	SER	A	38	8.165	16.820	24.641	1.00	44.87	A	C
ATOM	4	O	SER	A	38	7.431	17.426	23.855	1.00	44.76	A	O
ATOM	5	N	SER	A	38	6.339	15.165	24.930	1.00	47.40	A	N
ATOM	6	CA	SER	A	38	7.787	15.434	25.155	1.00	46.37	A	C
ATOM	7	N	HIS	A	39	9.311	17.315	25.099	1.00	42.59	A	N
ATOM	8	CA	HIS	A	39	9.807	18.631	24.708	1.00	40.15	A	C
ATOM	9	CB	HIS	A	39	10.759	19.164	25.780	1.00	43.57	A	C
ATOM	10	CG	HIS	A	39	11.980	18.320	25.978	1.00	46.37	A	C
ATOM	11	CD2	HIS	A	39	13.290	18.653	26.075	1.00	48.11	A	C
ATOM	12	ND1	HIS	A	39	11.923	16.950	26.124	1.00	48.60	A	N
ATOM	13	CE1	HIS	A	39	13.143	16.476	26.302	1.00	49.04	A	C
ATOM	14	NE2	HIS	A	39	13.992	17.489	26.276	1.00	48.92	A	N
ATOM	15	C	HIS	A	39	10.535	18.557	23.371	1.00	36.84	A	C
ATOM	16	O	HIS	A	39	11.370	17.680	23.157	1.00	36.46	A	O
ATOM	17	N	CYS	A	40	10.221	19.475	22.465	1.00	32.36	A	N
ATOM	18	CA	CYS	A	40	10.875	19.461	21.169	1.00	29.17	A	C
ATOM	19	C	CYS	A	40	12.286	20.011	21.292	1.00	26.49	A	C
ATOM	20	O	CYS	A	40	12.490	21.114	21.793	1.00	24.81	A	O
ATOM	21	CB	CYS	A	40	10.095	20.298	20.162	1.00	29.95	A	C
ATOM	22	SG	CYS	A	40	8.366	19.818	19.887	1.00	28.05	A	S
ATOM	23	N	ARG	A	41	13.259	19.238	20.828	1.00	24.42	A	N
ATOM	24	CA	ARG	A	41	14.648	19.657	20.890	1.00	24.30	A	C
ATOM	25	CB	ARG	A	41	15.144	19.580	22.339	1.00	28.36	A	C

```
ATOM     26  CG  ARG A  41      16.568  20.046  22.548  1.00 35.78
A    C
ATOM     27  CD  ARG A  41      16.733  20.673  23.927  1.00 40.37
A    C
ATOM     28  NE  ARG A  41      15.954  21.902  24.052  1.00 43.92
A    N
ATOM     29  CZ  ARG A  41      15.888  22.643  25.155  1.00 47.14
A    C
ATOM     30  NH1 ARG A  41      16.558  22.282  26.244  1.00 46.80
A    N
ATOM     31  NH2 ARG A  41      15.147  23.745  25.169  1.00 49.17
A    N
ATOM     32  C   ARG A  41      15.489  18.762  19.990  1.00 22.91
A    C
ATOM     33  O   ARG A  41      15.087  17.650  19.668  1.00 22.24
A    O
ATOM     34  N   LEU A  42      16.650  19.265  19.578  1.00 20.60
A    N
ATOM     35  CA  LEU A  42      17.568  18.528  18.715  1.00 17.57
A    C
ATOM     36  CB  LEU A  42      17.411  18.989  17.264  1.00 17.84
A    C
ATOM     37  CG  LEU A  42      16.086  18.717  16.557  1.00 18.08
A    C
ATOM     38  CD1 LEU A  42      16.074  19.406  15.195  1.00 17.09
A    C
ATOM     39  CD2 LEU A  42      15.902  17.218  16.405  1.00 18.48
A    C
ATOM     40  C   LEU A  42      18.992  18.814  19.184  1.00 16.85
A    C
ATOM     41  O   LEU A  42      19.391  19.973  19.306  1.00 18.05
A    O
ATOM     42  N   ASP A  43      19.760  17.766  19.455  1.00 15.30
A    N
ATOM     43  CA  ASP A  43      21.130  17.962  19.902  1.00 13.64
A    C
ATOM     44  CB  ASP A  43      21.815  16.607  20.093  1.00 13.53
A    C
ATOM     45  CG  ASP A  43      23.177  16.732  20.753  1.00 18.06
A    C
ATOM     46  OD1 ASP A  43      24.185  16.931  20.042  1.00 15.90
A    O
ATOM     47  OD2 ASP A  43      23.235  16.645  21.993  1.00 20.18
A    O
ATOM     48  C   ASP A  43      21.869  18.802  18.855  1.00 12.61
A    C
ATOM     49  O   ASP A  43      21.634  18.661  17.655  1.00 12.49
A    O
ATOM     50  N   LYS A  44      22.755  19.682  19.303  1.00 11.01
A    N
ATOM     51  CA  LYS A  44      23.497  20.525  18.373  1.00 11.24
A    C
ATOM     52  CB  LYS A  44      24.368  21.536  19.129  1.00 11.63
A    C
ATOM     53  CG  LYS A  44      24.903  22.642  18.219  1.00 14.43
A    C
ATOM     54  CD  LYS A  44      25.657  23.738  18.977  1.00 16.69
A    C
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ATOM     55  CE  LYS A  44      26.076  24.856  18.021  1.00 16.93
A    C
ATOM     56  NZ  LYS A  44      26.812  25.974  18.696  1.00 17.12
A    N
ATOM     57  C   LYS A  44      24.375  19.734  17.392  1.00 10.50
A    C
ATOM     58  O   LYS A  44      24.702  20.240  16.321  1.00 10.60
A    O
ATOM     59  N   SER A  45      24.753  18.507  17.745  1.00  8.11
A    N
ATOM     60  CA  SER A  45      25.585  17.699  16.844  1.00 10.59
A    C
ATOM     61  CB  SER A  45      25.941  16.352  17.479  1.00 10.95
A    C
ATOM     62  OG  SER A  45      24.779  15.624  17.827  1.00 12.31
A    O
ATOM     63  C   SER A  45      24.907  17.460  15.499  1.00 11.14
A    C
ATOM     64  O   SER A  45      25.571  17.208  14.496  1.00 10.24
A    O
ATOM     65  N   ASN A  46      23.582  17.533  15.477  1.00 10.77
A    N
ATOM     66  CA  ASN A  46      22.841  17.352  14.232  1.00 10.71
A    C
ATOM     67  CB  ASN A  46      21.335  17.486  14.476  1.00 10.57
A    C
ATOM     68  CG  ASN A  46      20.737  16.244  15.094  1.00 11.94
A    C
ATOM     69  OD1 ASN A  46      20.651  15.204  14.443  1.00 12.54
A    O
ATOM     70  ND2 ASN A  46      20.333  16.339  16.361  1.00  8.37
A    N
ATOM     71  C   ASN A  46      23.231  18.402  13.207  1.00 11.00
A    C
ATOM     72  O   ASN A  46      23.116  18.172  12.011  1.00 11.41
A    O
ATOM     73  N   PHE A  47      23.691  19.551  13.688  1.00 11.89
A    N
ATOM     74  CA  PHE A  47      24.028  20.671  12.812  1.00 13.43
A    C
ATOM     75  CB  PHE A  47      23.217  21.890  13.254  1.00 13.84
A    C
ATOM     76  CG  PHE A  47      21.760  21.593  13.463  1.00 13.84
A    C
ATOM     77  CD1 PHE A  47      20.886  21.510  12.377  1.00 15.85
A    C
ATOM     78  CD2 PHE A  47      21.273  21.347  14.739  1.00 12.02
A    C
ATOM     79  CE1 PHE A  47      19.543  21.182  12.567  1.00 15.39
A    C
ATOM     80  CE2 PHE A  47      19.937  21.019  14.940  1.00 14.91
A    C
ATOM     81  CZ  PHE A  47      19.068  20.935  13.855  1.00 12.76
A    C
ATOM     82  C   PHE A  47      25.498  21.047  12.773  1.00 12.62
A    C
ATOM     83  O   PHE A  47      25.846  22.136  12.312  1.00 13.52
A    O
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ATOM     84  N   GLN A  48      26.361  20.152  13.243  1.00 13.34
A    N
ATOM     85  CA  GLN A  48      27.789  20.436  13.281  1.00 12.80
A    C
ATOM     86  CB  GLN A  48      28.300  20.324  14.719  1.00 12.87
A    C
ATOM     87  CG  GLN A  48      27.678  21.326  15.686  1.00 14.56
A    C
ATOM     88  CD  GLN A  48      28.082  21.066  17.116  1.00 16.25
A    C
ATOM     89  OE1 GLN A  48      27.892  19.965  17.634  1.00 18.12
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ATOM     90  NE2 GLN A  48      28.644  22.075  17.766  1.00 15.04
A    N
ATOM     91  C   GLN A  48      28.636  19.542  12.388  1.00 14.54
A    C
ATOM     92  O   GLN A  48      29.860  19.568  12.486  1.00 13.57
A    O
ATOM     93  N   GLN A  49      27.998  18.749  11.528  1.00 12.16
A    N
ATOM     94  CA  GLN A  49      28.742  17.858  10.640  1.00 12.52
A    C
ATOM     95  CB  GLN A  49      27.990  16.530  10.503  1.00 12.58
A    C
ATOM     96  CG  GLN A  49      27.439  16.022  11.847  1.00 12.67
A    C
ATOM     97  CD  GLN A  49      28.483  16.019  12.961  1.00 15.57
A    C
ATOM     98  OE1 GLN A  49      29.730  15.772  12.598  1.00 12.50
A    O
ATOM     99  NE2 GLN A  49      28.165  16.234  14.136  1.00 14.24
A    N
ATOM    100  C   GLN A  49      28.941  18.568   9.295  1.00 12.85
A    C
ATOM    101  O   GLN A  49      27.985  18.899   8.589  1.00 11.22
A    O
ATOM    102  N   PRO A  50      30.204  18.823   8.927  1.00 13.42
A    N
ATOM    103  CD  PRO A  50      31.449  18.453   9.628  1.00 12.27
A    C
ATOM    104  CA  PRO A  50      30.492  19.514   7.666  1.00 12.60
A    C
ATOM    105  CB  PRO A  50      32.022  19.622   7.663  1.00 11.32
A    C
ATOM    106  CG  PRO A  50      32.460  18.448   8.495  1.00 14.19
A    C
ATOM    107  C   PRO A  50      29.948  18.944   6.370  1.00 11.49
A    C
ATOM    108  O   PRO A  50      29.464  19.697   5.520  1.00 10.14
A    O
ATOM    109  N   TYR A  51      30.001  17.629   6.205  1.00 11.00
A    N
ATOM    110  CA  TYR A  51      29.530  17.056   4.955  1.00 12.96
A    C
ATOM    111  CB  TYR A  51      29.750  15.535   4.932  1.00 14.28
A    C
ATOM    112  CG  TYR A  51      29.310  14.977   3.603  1.00 16.43
A    C
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ATOM    113  CD1 TYR A  51      30.152  15.062   2.498  1.00 16.36
A    C
ATOM    114  CE1 TYR A  51      29.742  14.584   1.244  1.00 18.58
A    C
ATOM    115  CD2 TYR A  51      28.041  14.386   3.425  1.00 17.28
A    C
ATOM    116  CE2 TYR A  51      27.619  13.935   2.175  1.00 17.57
A    C
ATOM    117  CZ  TYR A  51      28.476  14.041   1.089  1.00 19.05
A    C
ATOM    118  OH  TYR A  51      28.068  13.623  -0.157  1.00 20.18
A    O
ATOM    119  C   TYR A  51      28.068  17.375   4.634  1.00 11.00
A    C
ATOM    120  O   TYR A  51      27.773  17.999   3.612  1.00 12.39
A    O
ATOM    121  N   ILE A  52      27.159  16.938   5.494  1.00 10.51
A    N
ATOM    122  CA  ILE A  52      25.746  17.175   5.222  1.00 10.19
A    C
ATOM    123  CB  ILE A  52      24.838  16.307   6.125  1.00  7.95
A    C
ATOM    124  CG2 ILE A  52      24.850  16.814   7.558  1.00  7.43
A    C
ATOM    125  CG1 ILE A  52      23.427  16.282   5.537  1.00  9.73
A    C
ATOM    126  CD  ILE A  52      23.341  15.576   4.193  1.00  9.58
A    C
ATOM    127  C   ILE A  52      25.351  18.640   5.335  1.00  9.53
A    C
ATOM    128  O   ILE A  52      24.416  19.073   4.671  1.00 10.79
A    O
ATOM    129  N   THR A  53      26.053  19.407   6.167  1.00 10.80
A    N
ATOM    130  CA  THR A  53      25.739  20.828   6.293  1.00  9.84
A    C
ATOM    131  CB  THR A  53      26.507  21.481   7.459  1.00 11.16
A    C
ATOM    132  OG1 THR A  53      26.155  20.833   8.690  1.00 12.87
A    O
ATOM    133  CG2 THR A  53      26.163  22.967   7.554  1.00  9.20
A    C
ATOM    134  C   THR A  53      26.126  21.519   4.977  1.00 11.45
A    C
ATOM    135  O   THR A  53      25.410  22.387   4.479  1.00 11.63
A    O
ATOM    136  N   ASN A  54      27.257  21.114   4.407  1.00 13.24
A    N
ATOM    137  CA  ASN A  54      27.708  21.691   3.141  1.00 13.84
A    C
ATOM    138  CB  ASN A  54      29.105  21.170   2.785  1.00 14.48
A    C
ATOM    139  CG  ASN A  54      29.639  21.771   1.500  1.00 14.91
A    C
ATOM    140  OD1 ASN A  54      29.687  22.986   1.348  1.00 18.44
A    O
ATOM    141  ND2 ASN A  54      30.045  20.920   0.571  1.00 19.20
A    N
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ATOM    142  C   ASN A  54      26.719  21.350   2.025  1.00 12.10
A    C
ATOM    143  O   ASN A  54      26.380  22.200   1.205  1.00 13.81
A    O
ATOM    144  N   ARG A  55      26.260  20.102   1.997  1.00 14.14
A    N
ATOM    145  CA  ARG A  55      25.290  19.664   0.994  1.00 13.41
A    C
ATOM    146  CB  ARG A  55      24.950  18.180   1.176  1.00 15.87
A    C
ATOM    147  CG  ARG A  55      26.059  17.196   0.801  1.00 19.73
A    C
ATOM    148  CD  ARG A  55      26.505  17.386  -0.642  1.00 23.68
A    C
ATOM    149  NE  ARG A  55      27.405  16.325  -1.085  1.00 25.59
A    N
ATOM    150  CZ  ARG A  55      28.442  16.519  -1.891  1.00 27.42
A    C
ATOM    151  NH1 ARG A  55      28.710  17.733  -2.343  1.00 28.76
A    N
ATOM    152  NH2 ARG A  55      29.216  15.503  -2.241  1.00 27.48
A    N
ATOM    153  C   ARG A  55      24.007  20.480   1.129  1.00 11.99
A    C
ATOM    154  O   ARG A  55      23.412  20.893   0.134  1.00 11.77
A    O
ATOM    155  N   THR A  56      23.575  20.701   2.367  1.00 12.12
A    N
ATOM    156  CA  THR A  56      22.357  21.464   2.605  1.00 10.35
A    C
ATOM    157  CB  THR A  56      22.017  21.513   4.104  1.00 12.01
A    C
ATOM    158  OG1 THR A  56      21.792  20.180   4.591  1.00  7.11
A    O
ATOM    159  CG2 THR A  56      20.766  22.340   4.337  1.00  8.42
A    C
ATOM    160  C   THR A  56      22.483  22.889   2.062  1.00 12.24
A    C
ATOM    161  O   THR A  56      21.604  23.370   1.345  1.00  8.45
A    O
ATOM    162  N   PHE A  57      23.571  23.573   2.399  1.00 11.55
A    N
ATOM    163  CA  PHE A  57      23.753  24.937   1.914  1.00 12.54
A    C
ATOM    164  CB  PHE A  57      24.929  25.609   2.624  1.00 12.16
A    C
ATOM    165  CG  PHE A  57      24.568  26.181   3.960  1.00 13.36
A    C
ATOM    166  CD1 PHE A  57      24.313  25.354   5.046  1.00 13.15
A    C
ATOM    167  CD2 PHE A  57      24.464  27.553   4.130  1.00 14.39
A    C
ATOM    168  CE1 PHE A  57      23.961  25.887   6.282  1.00 14.05
A    C
ATOM    169  CE2 PHE A  57      24.113  28.092   5.359  1.00 12.06
A    C
ATOM    170  CZ  PHE A  57      23.862  27.259   6.438  1.00 13.80
A    C
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ATOM    171  C   PHE A  57      23.936  25.003   0.398  1.00 13.58
A    C
ATOM    172  O   PHE A  57      23.483  25.952  -0.244  1.00 13.09
A    O
ATOM    173  N   MET A  58      24.579  23.992  -0.177  1.00 13.90
A    N
ATOM    174  CA  MET A  58      24.782  23.969  -1.622  1.00 15.62
A    C
ATOM    175  CB  MET A  58      25.750  22.859  -2.019  1.00 16.17
A    C
ATOM    176  CG  MET A  58      27.164  23.047  -1.506  1.00 21.09
A    C
ATOM    177  SD  MET A  58      28.342  21.989  -2.379  1.00 27.56
A    S
ATOM    178  CE  MET A  58      27.683  20.368  -2.012  1.00 26.89
A    C
ATOM    179  C   MET A  58      23.454  23.759  -2.337  1.00 13.03
A    C
ATOM    180  O   MET A  58      23.215  24.322  -3.405  1.00 11.50
A    O
ATOM    181  N   LEU A  59      22.589  22.940  -1.749  1.00 12.01
A    N
ATOM    182  CA  LEU A  59      21.286  22.696  -2.347  1.00 12.06
A    C
ATOM    183  CB  LEU A  59      20.548  21.587  -1.597  1.00 12.51
A    C
ATOM    184  CG  LEU A  59      19.085  21.390  -2.012  1.00 13.80
A    C
ATOM    185  CD1 LEU A  59      18.991  21.124  -3.512  1.00 14.82
A    C
ATOM    186  CD2 LEU A  59      18.486  20.243  -1.225  1.00 10.84
A    C
ATOM    187  C   LEU A  59      20.474  23.990  -2.307  1.00 14.49
A    C
ATOM    188  O   LEU A  59      19.769  24.325  -3.262  1.00 13.13
A    O
ATOM    189  N   ALA A  60      20.578  24.718  -1.195  1.00 14.81
A    N
ATOM    190  CA  ALA A  60      19.857  25.974  -1.046  1.00 14.10
A    C
ATOM    191  CB  ALA A  60      20.077  26.545   0.344  1.00 14.30
A    C
ATOM    192  C   ALA A  60      20.339  26.963  -2.100  1.00 15.08
A    C
ATOM    193  O   ALA A  60      19.537  27.621  -2.761  1.00 12.89
A    O
ATOM    194  N   LYS A  61      21.654  27.065  -2.263  1.00 14.92
A    N
ATOM    195  CA  LYS A  61      22.209  27.985  -3.246  1.00 14.74
A    C
ATOM    196  CB  LYS A  61      23.740  27.926  -3.227  1.00 16.05
A    C
ATOM    197  CG  LYS A  61      24.421  28.890  -4.194  1.00 17.02
A    C
ATOM    198  CD  LYS A  61      24.047  30.325  -3.891  1.00 19.86
A    C
ATOM    199  CE  LYS A  61      24.717  31.288  -4.854  1.00 24.25
A    C
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ATOM    200  NZ  LYS A  61      24.367  32.697  -4.518  1.00 25.65
A    N
ATOM    201  C   LYS A  61      21.687  27.665  -4.642  1.00 15.27
A    C
ATOM    202  O   LYS A  61      21.161  28.537  -5.328  1.00 14.82
A    O
ATOM    203  N   GLU A  62      21.819  26.411  -5.057  1.00 15.81
A    N
ATOM    204  CA  GLU A  62      21.353  26.001  -6.373  1.00 18.42
A    C
ATOM    205  CB  GLU A  62      21.572  24.498  -6.555  1.00 20.56
A    C
ATOM    206  CG  GLU A  62      21.338  24.016  -7.969  1.00 27.23
A    C
ATOM    207  CD  GLU A  62      21.791  22.573  -8.214  1.00 31.47
A    C
ATOM    208  OE1 GLU A  62      22.875  22.136  -7.748  1.00 32.95
A    O
ATOM    209  OE2 GLU A  62      21.044  21.870  -8.914  1.00 33.23
A    O
ATOM    210  C   GLU A  62      19.879  26.348  -6.592  1.00 17.89
A    C
ATOM    211  O   GLU A  62      19.514  26.908  -7.625  1.00 16.93
A    O
ATOM    212  N   ALA A  63      19.029  26.021  -5.623  1.00 17.26
A    N
ATOM    213  CA  ALA A  63      17.605  26.316  -5.752  1.00 16.93
A    C
ATOM    214  CB  ALA A  63      16.832  25.692  -4.598  1.00 16.38
A    C
ATOM    215  C   ALA A  63      17.341  27.818  -5.801  1.00 17.17
A    C
ATOM    216  O   ALA A  63      16.477  28.280  -6.552  1.00 16.33
A    O
ATOM    217  N   SER A  64      18.079  28.586  -5.006  1.00 15.83
A    N
ATOM    218  CA  SER A  64      17.876  30.026  -4.992  1.00 18.51
A    C
ATOM    219  CB  SER A  64      18.748  30.686  -3.918  1.00 19.42
A    C
ATOM    220  OG  SER A  64      20.118  30.643  -4.267  1.00 21.79
A    O
ATOM    221  C   SER A  64      18.187  30.625  -6.364  1.00 19.15
A    C
ATOM    222  O   SER A  64      17.632  31.659  -6.739  1.00 18.21
A    O
ATOM    223  N   LEU A  65      19.067  29.966  -7.116  1.00 20.27
A    N
ATOM    224  CA  LEU A  65      19.433  30.454  -8.442  1.00 19.37
A    C
ATOM    225  CB  LEU A  65      20.727  29.797  -8.924  1.00 19.96
A    C
ATOM    226  CG  LEU A  65      22.002  30.321  -8.250  1.00 20.32
A    C
ATOM    227  CD1 LEU A  65      23.174  29.425  -8.604  1.00 21.39
A    C
ATOM    228  CD2 LEU A  65      22.268  31.752  -8.694  1.00 19.85
A    C
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ATOM    229  C   LEU A  65      18.317  30.182  -9.429  1.00 20.47
A    C
ATOM    230  O   LEU A  65      18.318  30.707 -10.545  1.00 19.18
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ATOM    231  N   ALA A  66      17.363  29.358  -9.010  1.00 18.96
A    N
ATOM    232  CA  ALA A  66      16.231  29.022  -9.859  1.00 20.12
A    C
ATOM    233  CB  ALA A  66      15.983  27.521  -9.822  1.00 19.46
A    C
ATOM    234  C   ALA A  66      14.989  29.775  -9.390  1.00 21.39
A    C
ATOM    235  O   ALA A  66      13.926  29.661  -9.985  1.00 20.75
A    O
ATOM    236  N   ASP A  67      15.141  30.560  -8.331  1.00 22.23
A    N
ATOM    237  CA  ASP A  67      14.036  31.320  -7.761  1.00 24.31
A    C
ATOM    238  CB  ASP A  67      14.022  31.084  -6.246  1.00 25.00
A    C
ATOM    239  CG  ASP A  67      13.134  32.055  -5.497  1.00 24.66
A    C
ATOM    240  OD1 ASP A  67      12.112  32.513  -6.056  1.00 24.92
A    O
ATOM    241  OD2 ASP A  67      13.465  32.341  -4.328  1.00 21.55
A    O
ATOM    242  C   ASP A  67      14.116  32.813  -8.083  1.00 25.59
A    C
ATOM    243  O   ASP A  67      15.012  33.511  -7.609  1.00 25.98
A    O
ATOM    244  N   ASN A  68      13.172  33.297  -8.889  1.00 27.63
A    N
ATOM    245  CA  ASN A  68      13.138  34.708  -9.271  1.00 30.16
A    C
ATOM    246  CB  ASN A  68      12.696  34.857 -10.731  1.00 32.04
A    C
ATOM    247  CG  ASN A  68      13.815  34.567 -11.710  1.00 35.26
A    C
ATOM    248  OD1 ASN A  68      14.891  35.160 -11.627  1.00 37.18
A    O
ATOM    249  ND2 ASN A  68      13.567  33.661 -12.651  1.00 36.56
A    N
ATOM    250  C   ASN A  68      12.245  35.585  -8.401  1.00 31.73
A    C
ATOM    251  O   ASN A  68      12.134  36.785  -8.649  1.00 31.89
A    O
ATOM    252  N   ASN A  69      11.586  34.992  -7.408  1.00 32.78
A    N
ATOM    253  CA  ASN A  69      10.698  35.744  -6.519  1.00 35.19
A    C
ATOM    254  CB  ASN A  69       9.746  34.801  -5.772  1.00 36.74
A    C
ATOM    255  CG  ASN A  69       9.056  33.805  -6.688  1.00 40.93
A    C
ATOM    256  OD1 ASN A  69       8.300  34.186  -7.586  1.00 41.57
A    O
ATOM    257  ND2 ASN A  69       9.311  32.515  -6.461  1.00 40.68
A    N
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ATOM	258	C	ASN	A	69	11.542	36.510	-5.501	1.00	35.09	A	C
ATOM	259	O	ASN	A	69	11.646	36.109	-4.339	1.00	32.29	A	O
ATOM	260	N	THR	A	70	12.134	37.615	-5.942	1.00	35.82	A	N
ATOM	261	CA	THR	A	70	12.979	38.430	-5.078	1.00	37.87	A	C
ATOM	262	CB	THR	A	70	13.852	39.386	-5.906	1.00	38.42	A	C
ATOM	263	OG1	THR	A	70	13.014	40.346	-6.555	1.00	38.69	A	O
ATOM	264	CG2	THR	A	70	14.631	38.623	-6.960	1.00	38.88	A	C
ATOM	265	C	THR	A	70	12.192	39.275	-4.072	1.00	38.60	A	C
ATOM	266	O	THR	A	70	12.781	39.904	-3.190	1.00	40.16	A	O
ATOM	267	N	ASP	A	71	10.868	39.282	-4.196	1.00	39.04	A	N
ATOM	268	CA	ASP	A	71	10.017	40.069	-3.305	1.00	39.32	A	C
ATOM	269	CB	ASP	A	71	8.838	40.662	-4.078	1.00	42.61	A	C
ATOM	270	CG	ASP	A	71	9.276	41.445	-5.281	1.00	47.01	A	C
ATOM	271	OD1	ASP	A	71	9.915	40.831	-6.152	1.00	49.64	A	O
ATOM	272	OD2	ASP	A	71	8.991	42.661	-5.362	1.00	50.35	A	O
ATOM	273	C	ASP	A	71	9.451	39.301	-2.119	1.00	37.56	A	C
ATOM	274	O	ASP	A	71	8.886	39.906	-1.206	1.00	37.36	A	O
ATOM	275	N	VAL	A	72	9.590	37.979	-2.128	1.00	33.02	A	N
ATOM	276	CA	VAL	A	72	9.040	37.171	-1.048	1.00	29.68	A	C
ATOM	277	CB	VAL	A	72	8.003	36.165	-1.590	1.00	31.44	A	C
ATOM	278	CG1	VAL	A	72	7.361	35.408	-0.437	1.00	31.76	A	C
ATOM	279	CG2	VAL	A	72	6.951	36.899	-2.416	1.00	34.37	A	C
ATOM	280	C	VAL	A	72	10.074	36.392	-0.252	1.00	26.18	A	C
ATOM	281	O	VAL	A	72	11.011	35.825	-0.814	1.00	24.53	A	O
ATOM	282	N	ARG	A	73	9.879	36.372	1.061	1.00	24.81	A	N
ATOM	283	CA	ARG	A	73	10.744	35.656	1.996	1.00	25.04	A	C
ATOM	284	CB	ARG	A	73	11.426	36.640	2.951	1.00	27.84	A	C
ATOM	285	CG	ARG	A	73	12.237	35.992	4.066	1.00	31.02	A	C
ATOM	286	CD	ARG	A	73	13.488	35.315	3.527	1.00	33.29	A	C

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ATOM    287  NE  ARG A  73      14.469  36.271   3.019  1.00 37.87
A    N
ATOM    288  CZ  ARG A  73      15.093  37.178   3.765  1.00 39.29
A    C
ATOM    289  NH1 ARG A  73      14.847  37.266   5.066  1.00 39.10
A    N
ATOM    290  NH2 ARG A  73      15.967  38.002   3.207  1.00 42.25
A    N
ATOM    291  C   ARG A  73       9.819  34.739   2.783  1.00 23.44
A    C
ATOM    292  O   ARG A  73       8.797  35.189   3.303  1.00 23.25
A    O
ATOM    293  N   LEU A  74      10.158  33.458   2.871  1.00 20.73
A    N
ATOM    294  CA  LEU A  74       9.311  32.522   3.602  1.00 18.25
A    C
ATOM    295  CB  LEU A  74       9.412  31.120   2.994  1.00 19.13
A    C
ATOM    296  CG  LEU A  74       8.937  30.973   1.546  1.00 19.57
A    C
ATOM    297  CD1 LEU A  74       9.020  29.523   1.122  1.00 19.10
A    C
ATOM    298  CD2 LEU A  74       7.504  31.462   1.420  1.00 19.94
A    C
ATOM    299  C   LEU A  74       9.655  32.466   5.081  1.00 18.81
A    C
ATOM    300  O   LEU A  74       8.772  32.562   5.930  1.00 17.72
A    O
ATOM    301  N   ILE A  75      10.940  32.307   5.391  1.00 17.09
A    N
ATOM    302  CA  ILE A  75      11.375  32.239   6.781  1.00 16.71
A    C
ATOM    303  CB  ILE A  75      12.503  31.195   6.948  1.00 17.07
A    C
ATOM    304  CG2 ILE A  75      13.077  31.258   8.361  1.00 17.86
A    C
ATOM    305  CG1 ILE A  75      11.950  29.798   6.642  1.00 18.78
A    C
ATOM    306  CD  ILE A  75      12.978  28.681   6.749  1.00 18.86
A    C
ATOM    307  C   ILE A  75      11.848  33.612   7.263  1.00 17.51
A    C
ATOM    308  O   ILE A  75      12.939  34.062   6.931  1.00 15.26
A    O
ATOM    309  N   GLY A  76      11.017  34.281   8.052  1.00 18.34
A    N
ATOM    310  CA  GLY A  76      11.389  35.600   8.530  1.00 21.35
A    C
ATOM    311  C   GLY A  76      10.608  36.007   9.761  1.00 23.15
A    C
ATOM    312  O   GLY A  76       9.916  35.187  10.357  1.00 21.36
A    O
ATOM    313  N   GLU A  77      10.706  37.282  10.125  1.00 26.14
A    N
ATOM    314  CA  GLU A  77      10.043  37.817  11.313  1.00 27.91
A    C
ATOM    315  CB  GLU A  77      10.118  39.349  11.300  1.00 31.26
A    C
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ATOM    316  CG  GLU A  77       9.551  40.011  12.548  1.00 36.17
A    C
ATOM    317  CD  GLU A  77       9.807  41.508  12.584  1.00 39.76
A    C
ATOM    318  OE1 GLU A  77       9.440  42.203  11.609  1.00 39.06
A    O
ATOM    319  OE2 GLU A  77      10.375  41.986  13.591  1.00 41.22
A    O
ATOM    320  C   GLU A  77       8.595  37.370  11.517  1.00 27.70
A    C
ATOM    321  O   GLU A  77       8.235  36.899  12.595  1.00 28.81
A    O
ATOM    322  N   LYS A  78       7.767  37.514  10.491  1.00 27.14
A    N
ATOM    323  CA  LYS A  78       6.364  37.125  10.594  1.00 26.90
A    C
ATOM    324  CB  LYS A  78       5.652  37.351   9.254  1.00 29.37
A    C
ATOM    325  CG  LYS A  78       6.481  36.998   8.023  1.00 34.70
A    C
ATOM    326  CD  LYS A  78       7.597  38.018   7.773  1.00 35.71
A    C
ATOM    327  CE  LYS A  78       8.457  37.619   6.584  1.00 37.67
A    C
ATOM    328  NZ  LYS A  78       9.458  38.670   6.251  1.00 39.35
A    N
ATOM    329  C   LYS A  78       6.147  35.688  11.061  1.00 24.99
A    C
ATOM    330  O   LYS A  78       5.244  35.419  11.850  1.00 24.73
A    O
ATOM    331  N   LEU A  79       6.974  34.765  10.580  1.00 23.10
A    N
ATOM    332  CA  LEU A  79       6.851  33.360  10.954  1.00 21.97
A    C
ATOM    333  CB  LEU A  79       7.903  32.533  10.206  1.00 21.38
A    C
ATOM    334  CG  LEU A  79       7.963  31.034  10.510  1.00 19.79
A    C
ATOM    335  CD1 LEU A  79       6.618  30.386  10.186  1.00 18.36
A    C
ATOM    336  CD2 LEU A  79       9.076  30.395   9.688  1.00 18.38
A    C
ATOM    337  C   LEU A  79       7.005  33.126  12.457  1.00 22.48
A    C
ATOM    338  O   LEU A  79       6.378  32.232  13.026  1.00 21.54
A    O
ATOM    339  N   PHE A  80       7.839  33.936  13.098  1.00 24.35
A    N
ATOM    340  CA  PHE A  80       8.102  33.799  14.525  1.00 25.81
A    C
ATOM    341  CB  PHE A  80       9.599  33.972  14.768  1.00 24.41
A    C
ATOM    342  CG  PHE A  80      10.447  33.009  13.990  1.00 24.03
A    C
ATOM    343  CD1 PHE A  80      10.510  31.667  14.351  1.00 23.62
A    C
ATOM    344  CD2 PHE A  80      11.158  33.437  12.875  1.00 23.15
A    C
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ATOM    345  CE1 PHE A  80      11.270  30.759  13.606  1.00 23.39
A    C
ATOM    346  CE2 PHE A  80      11.917  32.543  12.125  1.00 23.09
A    C
ATOM    347  CZ  PHE A  80      11.974  31.200  12.491  1.00 23.28
A    C
ATOM    348  C   PHE A  80       7.324  34.775  15.410  1.00 28.55
A    C
ATOM    349  O   PHE A  80       7.362  34.676  16.637  1.00 28.74
A    O
ATOM    350  N   HIS A  81       6.618  35.711  14.787  1.00 30.56
A    N
ATOM    351  CA  HIS A  81       5.849  36.711  15.519  1.00 32.02
A    C
ATOM    352  CB  HIS A  81       5.051  37.579  14.540  1.00 34.06
A    C
ATOM    353  CG  HIS A  81       4.321  38.711  15.193  1.00 36.89
A    C
ATOM    354  CD2 HIS A  81       2.996  38.959  15.325  1.00 37.63
A    C
ATOM    355  ND1 HIS A  81       4.971  39.748  15.829  1.00 38.12
A    N
ATOM    356  CE1 HIS A  81       4.078  40.585  16.325  1.00 38.01
A    C
ATOM    357  NE2 HIS A  81       2.873  40.129  16.033  1.00 38.42
A    N
ATOM    358  C   HIS A  81       4.902  36.097  16.547  1.00 30.87
A    C
ATOM    359  O   HIS A  81       4.060  35.268  16.211  1.00 32.80
A    O
ATOM    360  N   GLY A  82       5.046  36.511  17.802  1.00 30.56
A    N
ATOM    361  CA  GLY A  82       4.192  35.997  18.859  1.00 29.32
A    C
ATOM    362  C   GLY A  82       4.593  34.640  19.420  1.00 28.91
A    C
ATOM    363  O   GLY A  82       3.989  34.165  20.380  1.00 29.61
A    O
ATOM    364  N   VAL A  83       5.609  34.011  18.835  1.00 26.58
A    N
ATOM    365  CA  VAL A  83       6.064  32.697  19.295  1.00 24.46
A    C
ATOM    366  CB  VAL A  83       6.569  31.855  18.096  1.00 24.84
A    C
ATOM    367  CG1 VAL A  83       6.971  30.470  18.531  1.00 24.49
A    C
ATOM    368  CG2 VAL A  83       5.480  31.749  17.066  1.00 24.95
A    C
ATOM    369  C   VAL A  83       7.180  32.847  20.328  1.00 23.20
A    C
ATOM    370  O   VAL A  83       8.218  33.429  20.043  1.00 20.58
A    O
ATOM    371  N   SER A  84       6.956  32.336  21.535  1.00 22.74
A    N
ATOM    372  CA  SER A  84       7.961  32.427  22.586  1.00 22.59
A    C
ATOM    373  CB  SER A  84       7.325  32.136  23.942  1.00 24.87
A    C
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ATOM    374  OG  SER A  84       6.740  30.847  23.960  1.00 28.28
A    O
ATOM    375  C   SER A  84       9.091  31.438  22.319  1.00 22.22
A    C
ATOM    376  O   SER A  84       8.891  30.428  21.649  1.00 19.25
A    O
ATOM    377  N   MET A  85      10.271  31.723  22.860  1.00 22.89
A    N
ATOM    378  CA  MET A  85      11.438  30.864  22.661  1.00 23.51
A    C
ATOM    379  CB  MET A  85      12.626  31.391  23.470  1.00 26.40
A    C
ATOM    380  CG  MET A  85      12.965  32.850  23.205  1.00 32.22
A    C
ATOM    381  SD  MET A  85      13.130  33.234  21.443  1.00 38.24
A    S
ATOM    382  CE  MET A  85      11.634  34.156  21.178  1.00 39.11
A    C
ATOM    383  C   MET A  85      11.213  29.391  23.010  1.00 21.82
A    C
ATOM    384  O   MET A  85      11.799  28.506  22.387  1.00 21.96
A    O
ATOM    385  N   SER A  86      10.377  29.121  24.006  1.00 20.05
A    N
ATOM    386  CA  SER A  86      10.123  27.743  24.405  1.00 20.16
A    C
ATOM    387  CB  SER A  86       9.504  27.701  25.801  1.00 20.31
A    C
ATOM    388  OG  SER A  86       8.281  28.406  25.816  1.00 19.38
A    O
ATOM    389  C   SER A  86       9.215  26.993  23.436  1.00 20.16
A    C
ATOM    390  O   SER A  86       9.039  25.780  23.563  1.00 21.23
A    O
ATOM    391  N   GLU A  87       8.633  27.702  22.475  1.00 18.55
A    N
ATOM    392  CA  GLU A  87       7.757  27.044  21.505  1.00 19.19
A    C
ATOM    393  CB  GLU A  87       6.381  27.717  21.480  1.00 21.48
A    C
ATOM    394  CG  GLU A  87       5.848  28.071  22.849  1.00 27.63
A    C
ATOM    395  CD  GLU A  87       4.583  28.925  22.796  1.00 30.13
A    C
ATOM    396  OE1 GLU A  87       4.609  30.033  22.220  1.00 30.21
A    O
ATOM    397  OE2 GLU A  87       3.553  28.497  23.344  1.00 33.94
A    O
ATOM    398  C   GLU A  87       8.337  27.066  20.095  1.00 17.25
A    C
ATOM    399  O   GLU A  87       7.786  26.443  19.189  1.00 15.95
A    O
ATOM    400  N   ARG A  88       9.447  27.778  19.910  1.00 16.02
A    N
ATOM    401  CA  ARG A  88      10.081  27.887  18.599  1.00 15.63
A    C
ATOM    402  CB  ARG A  88      11.356  28.729  18.693  1.00 18.69
A    C
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ATOM    403  CG  ARG A  88      11.146  30.190  19.067  1.00 23.67
A    C
ATOM    404  CD  ARG A  88      10.457  30.944  17.961  1.00 26.36
A    C
ATOM    405  NE  ARG A  88      10.175  32.337  18.311  1.00 30.28
A    N
ATOM    406  CZ  ARG A  88      11.044  33.337  18.206  1.00 31.77
A    C
ATOM    407  NH1 ARG A  88      12.270  33.111  17.762  1.00 34.62
A    N
ATOM    408  NH2 ARG A  88      10.678  34.574  18.518  1.00 30.69
A    N
ATOM    409  C   ARG A  88      10.423  26.541  17.951  1.00 15.43
A    C
ATOM    410  O   ARG A  88      10.153  26.333  16.767  1.00 15.17
A    O
ATOM    411  N   CYS A  89      11.025  25.628  18.708  1.00 12.14
A    N
ATOM    412  CA  CYS A  89      11.381  24.342  18.120  1.00 13.07
A    C
ATOM    413  C   CYS A  89      10.133  23.605  17.611  1.00 14.78
A    C
ATOM    414  O   CYS A  89      10.158  23.020  16.528  1.00 13.46
A    O
ATOM    415  CB  CYS A  89      12.169  23.472  19.107  1.00 12.57
A    C
ATOM    416  SG  CYS A  89      12.780  21.964  18.306  1.00 15.35
A    S
ATOM    417  N   TYR A  90       9.044  23.653  18.378  1.00 13.52
A    N
ATOM    418  CA  TYR A  90       7.789  23.017  17.970  1.00 14.36
A    C
ATOM    419  CB  TYR A  90       6.729  23.149  19.063  1.00 16.25
A    C
ATOM    420  CG  TYR A  90       5.386  22.598  18.640  1.00 20.73
A    C
ATOM    421  CD1 TYR A  90       5.172  21.220  18.551  1.00 22.84
A    C
ATOM    422  CE1 TYR A  90       3.936  20.704  18.142  1.00 25.51
A    C
ATOM    423  CD2 TYR A  90       4.334  23.453  18.308  1.00 21.97
A    C
ATOM    424  CE2 TYR A  90       3.095  22.947  17.894  1.00 25.27
A    C
ATOM    425  CZ  TYR A  90       2.908  21.575  17.813  1.00 26.64
A    C
ATOM    426  OH  TYR A  90       1.698  21.073  17.393  1.00 31.95
A    O
ATOM    427  C   TYR A  90       7.283  23.691  16.699  1.00 12.19
A    C
ATOM    428  O   TYR A  90       6.762  23.032  15.797  1.00 13.82
A    O
ATOM    429  N   LEU A  91       7.430  25.011  16.630  1.00 13.87
A    N
ATOM    430  CA  LEU A  91       7.020  25.763  15.445  1.00 14.25
A    C
ATOM    431  CB  LEU A  91       7.279  27.259  15.657  1.00 16.00
A    C
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ATOM    432  CG  LEU A  91       7.389  28.125  14.403  1.00 20.38
A    C
ATOM    433  CD1 LEU A  91       6.049  28.180  13.691  1.00 20.90
A    C
ATOM    434  CD2 LEU A  91       7.848  29.522  14.795  1.00 23.19
A    C
ATOM    435  C   LEU A  91       7.841  25.271  14.250  1.00 14.26
A    C
ATOM    436  O   LEU A  91       7.298  25.011  13.166  1.00 13.95
A    O
ATOM    437  N   MET A  92       9.156  25.144  14.454  1.00 13.32
A    N
ATOM    438  CA  MET A  92      10.054  24.693  13.386  1.00 12.34
A    C
ATOM    439  CB  MET A  92      11.520  24.855  13.791  1.00 13.46
A    C
ATOM    440  CG  MET A  92      11.943  26.329  13.855  1.00 13.93
A    C
ATOM    441  SD  MET A  92      11.513  27.272  12.365  1.00 19.44
A    S
ATOM    442  CE  MET A  92      12.398  26.314  11.091  1.00 16.94
A    C
ATOM    443  C   MET A  92       9.763  23.272  12.941  1.00 13.49
A    C
ATOM    444  O   MET A  92       9.975  22.924  11.777  1.00 14.17
A    O
ATOM    445  N   LYS A  93       9.255  22.465  13.864  1.00 12.98
A    N
ATOM    446  CA  LYS A  93       8.889  21.097  13.557  1.00 13.82
A    C
ATOM    447  CB  LYS A  93       8.385  20.395  14.810  1.00 13.12
A    C
ATOM    448  CG  LYS A  93       7.672  19.082  14.522  1.00 18.61
A    C
ATOM    449  CD  LYS A  93       6.889  18.604  15.736  1.00 18.28
A    C
ATOM    450  CE  LYS A  93       6.085  17.352  15.441  1.00 20.53
A    C
ATOM    451  NZ  LYS A  93       5.352  16.889  16.657  1.00 19.33
A    N
ATOM    452  C   LYS A  93       7.770  21.124  12.526  1.00 13.87
A    C
ATOM    453  O   LYS A  93       7.760  20.328  11.593  1.00 15.68
A    O
ATOM    454  N   GLN A  94       6.823  22.043  12.700  1.00 15.16
A    N
ATOM    455  CA  GLN A  94       5.692  22.144  11.778  1.00 15.15
A    C
ATOM    456  CB  GLN A  94       4.630  23.089  12.344  1.00 17.59
A    C
ATOM    457  CG  GLN A  94       4.254  22.779  13.786  1.00 23.02
A    C
ATOM    458  CD  GLN A  94       3.713  21.376  13.964  1.00 25.41
A    C
ATOM    459  OE1 GLN A  94       3.829  20.788  15.038  1.00 31.14
A    O
ATOM    460  NE2 GLN A  94       3.110  20.836  12.917  1.00 25.01
A    N
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ATOM    461  C   GLN A  94       6.157  22.644  10.419  1.00 13.97
A    C
ATOM    462  O   GLN A  94       5.687  22.179   9.378  1.00 13.38
A    O
ATOM    463  N   VAL A  95       7.082  23.599  10.429  1.00 12.42
A    N
ATOM    464  CA  VAL A  95       7.598  24.140   9.183  1.00 11.71
A    C
ATOM    465  CB  VAL A  95       8.539  25.324   9.420  1.00 12.14
A    C
ATOM    466  CG1 VAL A  95       9.180  25.740   8.107  1.00 13.43
A    C
ATOM    467  CG2 VAL A  95       7.767  26.483   9.997  1.00 12.64
A    C
ATOM    468  C   VAL A  95       8.373  23.060   8.452  1.00 12.55
A    C
ATOM    469  O   VAL A  95       8.269  22.930   7.232  1.00 10.70
A    O
ATOM    470  N   LEU A  96       9.150  22.287   9.210  1.00 11.35
A    N
ATOM    471  CA  LEU A  96       9.953  21.212   8.639  1.00  9.86
A    C
ATOM    472  CB  LEU A  96      10.822  20.559   9.712  1.00 10.52
A    C
ATOM    473  CG  LEU A  96      11.572  19.302   9.248  1.00 12.76
A    C
ATOM    474  CD1 LEU A  96      12.575  19.657   8.158  1.00 11.47
A    C
ATOM    475  CD2 LEU A  96      12.282  18.662  10.445  1.00 11.92
A    C
ATOM    476  C   LEU A  96       9.088  20.145   7.994  1.00 10.33
A    C
ATOM    477  O   LEU A  96       9.327  19.751   6.855  1.00 10.88
A    O
ATOM    478  N   ASN A  97       8.086  19.669   8.725  1.00 11.10
A    N
ATOM    479  CA  ASN A  97       7.215  18.630   8.192  1.00 12.58
A    C
ATOM    480  CB  ASN A  97       6.270  18.130   9.290  1.00 15.76
A    C
ATOM    481  CG  ASN A  97       7.013  17.361  10.377  1.00 16.70
A    C
ATOM    482  OD1 ASN A  97       8.146  16.920  10.168  1.00 19.35
A    O
ATOM    483  ND2 ASN A  97       6.380  17.182  11.525  1.00 17.01
A    N
ATOM    484  C   ASN A  97       6.462  19.114   6.964  1.00 11.81
A    C
ATOM    485  O   ASN A  97       6.281  18.361   6.006  1.00 12.10
A    O
ATOM    486  N   PHE A  98       6.037  20.374   6.971  1.00 12.85
A    N
ATOM    487  CA  PHE A  98       5.347  20.917   5.806  1.00 13.45
A    C
ATOM    488  CB  PHE A  98       4.907  22.357   6.052  1.00 14.09
A    C
ATOM    489  CG  PHE A  98       4.623  23.121   4.788  1.00 17.24
A    C
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ATOM    490  CD1 PHE A  98       3.535  22.793   3.986  1.00 18.81
A    C
ATOM    491  CD2 PHE A  98       5.472  24.141   4.378  1.00 18.95
A    C
ATOM    492  CE1 PHE A  98       3.301  23.469   2.790  1.00 19.48
A    C
ATOM    493  CE2 PHE A  98       5.247  24.820   3.188  1.00 18.82
A    C
ATOM    494  CZ  PHE A  98       4.163  24.484   2.392  1.00 18.93
A    C
ATOM    495  C   PHE A  98       6.316  20.906   4.629  1.00 13.98
A    C
ATOM    496  O   PHE A  98       5.991  20.458   3.519  1.00 12.54
A    O
ATOM    497  N   THR A  99       7.519  21.405   4.878  1.00 12.46
A    N
ATOM    498  CA  THR A  99       8.509  21.473   3.818  1.00 12.12
A    C
ATOM    499  CB  THR A  99       9.789  22.174   4.297  1.00 13.25
A    C
ATOM    500  OG1 THR A  99       9.459  23.469   4.825  1.00 11.71
A    O
ATOM    501  CG2 THR A  99      10.745  22.345   3.137  1.00 12.11
A    C
ATOM    502  C   THR A  99       8.852  20.099   3.260  1.00 11.68
A    C
ATOM    503  O   THR A  99       9.081  19.950   2.061  1.00 12.57
A    O
ATOM    504  N   LEU A 100       8.892  19.092   4.124  1.00 12.47
A    N
ATOM    505  CA  LEU A 100       9.189  17.741   3.668  1.00 13.58
A    C
ATOM    506  CB  LEU A 100       9.405  16.817   4.870  1.00 13.64
A    C
ATOM    507  CG  LEU A 100      10.794  16.844   5.519  1.00 14.13
A    C
ATOM    508  CD1 LEU A 100      10.766  16.117   6.859  1.00 15.07
A    C
ATOM    509  CD2 LEU A 100      11.788  16.191   4.583  1.00 11.06
A    C
ATOM    510  C   LEU A 100       8.056  17.179   2.802  1.00 15.63
A    C
ATOM    511  O   LEU A 100       8.285  16.726   1.684  1.00 14.71
A    O
ATOM    512  N   GLU A 101       6.838  17.223   3.332  1.00 15.43
A    N
ATOM    513  CA  GLU A 101       5.660  16.687   2.656  1.00 17.18
A    C
ATOM    514  CB  GLU A 101       4.467  16.670   3.618  1.00 18.69
A    C
ATOM    515  CG  GLU A 101       4.530  15.627   4.730  1.00 22.02
A    C
ATOM    516  CD  GLU A 101       4.465  14.207   4.212  1.00 26.32
A    C
ATOM    517  OE1 GLU A 101       3.657  13.940   3.299  1.00 27.27
A    O
ATOM    518  OE2 GLU A 101       5.212  13.344   4.724  1.00 29.94
A    O
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ATOM    519  C   GLU A 101       5.220  17.375   1.370  1.00 17.32
A    C
ATOM    520  O   GLU A 101       4.913  16.706   0.378  1.00 17.41
A    O
ATOM    521  N   GLU A 102       5.194  18.702   1.378  1.00 16.65
A    N
ATOM    522  CA  GLU A 102       4.725  19.442   0.212  1.00 16.41
A    C
ATOM    523  CB  GLU A 102       3.629  20.402   0.657  1.00 19.20
A    C
ATOM    524  CG  GLU A 102       2.440  19.644   1.233  1.00 23.30
A    C
ATOM    525  CD  GLU A 102       1.369  20.554   1.771  1.00 26.38
A    C
ATOM    526  OE1 GLU A 102       0.828  21.357   0.981  1.00 25.51
A    O
ATOM    527  OE2 GLU A 102       1.073  20.465   2.984  1.00 27.95
A    O
ATOM    528  C   GLU A 102       5.745  20.170  -0.650  1.00 16.28
A    C
ATOM    529  O   GLU A 102       5.385  20.783  -1.653  1.00 14.86
A    O
ATOM    530  N   VAL A 103       7.015  20.109  -0.271  1.00 12.43
A    N
ATOM    531  CA  VAL A 103       8.045  20.755  -1.077  1.00 13.07
A    C
ATOM    532  CB  VAL A 103       8.742  21.907  -0.320  1.00 12.76
A    C
ATOM    533  CG1 VAL A 103       9.889  22.458  -1.162  1.00 12.19
A    C
ATOM    534  CG2 VAL A 103       7.753  23.024  -0.027  1.00 13.33
A    C
ATOM    535  C   VAL A 103       9.122  19.763  -1.509  1.00 13.14
A    C
ATOM    536  O   VAL A 103       9.271  19.462  -2.690  1.00 13.73
A    O
ATOM    537  N   LEU A 104       9.863  19.248  -0.538  1.00 12.65
A    N
ATOM    538  CA  LEU A 104      10.952  18.330  -0.824  1.00 14.40
A    C
ATOM    539  CB  LEU A 104      11.785  18.113   0.441  1.00 14.50
A    C
ATOM    540  CG  LEU A 104      12.438  19.396   0.972  1.00 14.36
A    C
ATOM    541  CD1 LEU A 104      13.126  19.115   2.295  1.00 15.72
A    C
ATOM    542  CD2 LEU A 104      13.441  19.928  -0.050  1.00 14.39
A    C
ATOM    543  C   LEU A 104      10.544  16.989  -1.415  1.00 15.37
A    C
ATOM    544  O   LEU A 104      11.215  16.480  -2.313  1.00 12.81
A    O
ATOM    545  N   PHE A 105       9.467  16.399  -0.916  1.00 15.46
A    N
ATOM    546  CA  PHE A 105       9.054  15.115  -1.466  1.00 17.77
A    C
ATOM    547  CB  PHE A 105       7.926  14.508  -0.621  1.00 18.57
A    C
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ATOM    548  CG  PHE A 105       8.400  13.952   0.706  1.00 20.35
A    C
ATOM    549  CD1 PHE A 105       9.750  14.016   1.066  1.00 22.06
A    C
ATOM    550  CD2 PHE A 105       7.505  13.366   1.590  1.00 21.24
A    C
ATOM    551  CE1 PHE A 105      10.193  13.501   2.288  1.00 22.72
A    C
ATOM    552  CE2 PHE A 105       7.935  12.847   2.817  1.00 21.30
A    C
ATOM    553  CZ  PHE A 105       9.280  12.914   3.168  1.00 24.04
A    C
ATOM    554  C   PHE A 105       8.658  15.282  -2.935  1.00 17.82
A    C
ATOM    555  O   PHE A 105       9.150  14.549  -3.798  1.00 17.32
A    O
ATOM    556  N   PRO A 106       7.788  16.263  -3.244  1.00 19.25
A    N
ATOM    557  CD  PRO A 106       6.995  17.100  -2.323  1.00 18.44
A    C
ATOM    558  CA  PRO A 106       7.372  16.487  -4.634  1.00 19.95
A    C
ATOM    559  CB  PRO A 106       6.417  17.672  -4.521  1.00 20.31
A    C
ATOM    560  CG  PRO A 106       5.806  17.480  -3.174  1.00 19.88
A    C
ATOM    561  C   PRO A 106       8.563  16.800  -5.541  1.00 20.82
A    C
ATOM    562  O   PRO A 106       8.553  16.483  -6.734  1.00 19.57
A    O
ATOM    563  N   GLN A 107       9.593  17.417  -4.964  1.00 21.36
A    N
ATOM    564  CA  GLN A 107      10.791  17.800  -5.714  1.00 21.96
A    C
ATOM    565  CB  GLN A 107      11.198  19.233  -5.335  1.00 22.81
A    C
ATOM    566  CG  GLN A 107      10.156  20.298  -5.638  1.00 24.02
A    C
ATOM    567  CD  GLN A 107      10.184  20.735  -7.086  1.00 27.15
A    C
ATOM    568  OE1 GLN A 107       9.302  21.459  -7.547  1.00 28.19
A    O
ATOM    569  NE2 GLN A 107      11.211  20.306  -7.811  1.00 27.09
A    N
ATOM    570  C   GLN A 107      11.968  16.872  -5.438  1.00 22.05
A    C
ATOM    571  O   GLN A 107      13.090  17.145  -5.871  1.00 21.11
A    O
ATOM    572  N   SER A 108      11.709  15.773  -4.734  1.00 22.40
A    N
ATOM    573  CA  SER A 108      12.756  14.829  -4.342  1.00 24.12
A    C
ATOM    574  CB  SER A 108      12.142  13.665  -3.559  1.00 21.76
A    C
ATOM    575  OG  SER A 108      11.263  12.909  -4.370  1.00 25.11
A    O
ATOM    576  C   SER A 108      13.667  14.276  -5.434  1.00 25.68
A    C
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ATOM    577  O   SER A 108      14.823  13.942  -5.168  1.00 25.48
A    O
ATOM    578  N   ASP A 109      13.165  14.179  -6.658  1.00 28.58
A    N
ATOM    579  CA  ASP A 109      13.976  13.654  -7.750  1.00 29.53
A    C
ATOM    580  CB  ASP A 109      13.131  12.719  -8.623  1.00 31.30
A    C
ATOM    581  CG  ASP A 109      11.897  13.398  -9.189  1.00 33.47
A    C
ATOM    582  OD1 ASP A 109      11.371  14.328  -8.542  1.00 33.88
A    O
ATOM    583  OD2 ASP A 109      11.443  12.987 -10.278  1.00 33.45
A    O
ATOM    584  C   ASP A 109      14.587  14.765  -8.593  1.00 30.64
A    C
ATOM    585  O   ASP A 109      15.058  14.527  -9.706  1.00 32.81
A    O
ATOM    586  N   ARG A 110      14.592  15.979  -8.050  1.00 29.79
A    N
ATOM    587  CA  ARG A 110      15.145  17.134  -8.748  1.00 28.46
A    C
ATOM    588  CB  ARG A 110      14.107  18.251  -8.819  1.00 31.87
A    C
ATOM    589  CG  ARG A 110      14.497  19.382  -9.753  1.00 37.18
A    C
ATOM    590  CD  ARG A 110      13.655  19.374 -11.020  1.00 41.24
A    C
ATOM    591  NE  ARG A 110      12.340  19.974 -10.803  1.00 43.98
A    N
ATOM    592  CZ  ARG A 110      12.146  21.255 -10.497  1.00 44.48
A    C
ATOM    593  NH1 ARG A 110      13.180  22.074 -10.373  1.00 44.65
A    N
ATOM    594  NH2 ARG A 110      10.916  21.718 -10.315  1.00 45.63
A    N
ATOM    595  C   ARG A 110      16.384  17.629  -8.008  1.00 25.45
A    C
ATOM    596  O   ARG A 110      16.715  17.118  -6.942  1.00 25.04
A    O
ATOM    597  N   PHE A 111      17.070  18.616  -8.576  1.00 22.98
A    N
ATOM    598  CA  PHE A 111      18.278  19.163  -7.965  1.00 22.26
A    C
ATOM    599  CB  PHE A 111      17.900  20.022  -6.749  1.00 21.90
A    C
ATOM    600  CG  PHE A 111      17.148  21.274  -7.111  1.00 18.30
A    C
ATOM    601  CD1 PHE A 111      17.795  22.325  -7.747  1.00 20.61
A    C
ATOM    602  CD2 PHE A 111      15.793  21.381  -6.866  1.00 19.71
A    C
ATOM    603  CE1 PHE A 111      17.101  23.461  -8.135  1.00 20.07
A    C
ATOM    604  CE2 PHE A 111      15.085  22.520  -7.254  1.00 20.77
A    C
ATOM    605  CZ  PHE A 111      15.742  23.557  -7.890  1.00 22.06
A    C
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ATOM    606  C   PHE A 111      19.281  18.070  -7.561  1.00 23.53
A    C
ATOM    607  O   PHE A 111      19.819  18.082  -6.453  1.00 21.50
A    O
ATOM    608  N   GLN A 112      19.528  17.125  -8.468  1.00 24.20
A    N
ATOM    609  CA  GLN A 112      20.486  16.042  -8.215  1.00 24.96
A    C
ATOM    610  CB  GLN A 112      20.397  14.962  -9.304  1.00 27.91
A    C
ATOM    611  CG  GLN A 112      19.033  14.309  -9.375  1.00 32.20
A    C
ATOM    612  CD  GLN A 112      18.866  13.316 -10.503  1.00 36.00
A    C
ATOM    613  OE1 GLN A 112      17.772  12.806 -10.719  1.00 37.02
A    O
ATOM    614  NE2 GLN A 112      19.946  13.033 -11.225  1.00 37.13
A    N
ATOM    615  C   GLN A 112      21.897  16.630  -8.196  1.00 26.21
A    C
ATOM    616  O   GLN A 112      22.184  17.597  -8.908  1.00 27.42
A    O
ATOM    617  N   PRO A 113      22.806  16.047  -7.392  1.00 25.53
A    N
ATOM    618  CD  PRO A 113      24.251  16.272  -7.577  1.00 25.70
A    C
ATOM    619  CA  PRO A 113      22.577  14.900  -6.506  1.00 25.89
A    C
ATOM    620  CB  PRO A 113      23.853  14.098  -6.695  1.00 26.16
A    C
ATOM    621  CG  PRO A 113      24.876  15.203  -6.687  1.00 25.44
A    C
ATOM    622  C   PRO A 113      22.385  15.287  -5.032  1.00 25.87
A    C
ATOM    623  O   PRO A 113      22.095  14.434  -4.195  1.00 25.05
A    O
ATOM    624  N   TYR A 114      22.541  16.571  -4.717  1.00 26.68
A    N
ATOM    625  CA  TYR A 114      22.430  17.029  -3.331  1.00 27.34
A    C
ATOM    626  CB  TYR A 114      22.838  18.510  -3.228  1.00 30.74
A    C
ATOM    627  CG  TYR A 114      24.167  18.813  -3.898  1.00 33.96
A    C
ATOM    628  CD1 TYR A 114      25.228  17.916  -3.804  1.00 36.01
A    C
ATOM    629  CE1 TYR A 114      26.435  18.161  -4.438  1.00 38.72
A    C
ATOM    630  CD2 TYR A 114      24.354  19.979  -4.648  1.00 35.86
A    C
ATOM    631  CE2 TYR A 114      25.568  20.238  -5.290  1.00 37.49
A    C
ATOM    632  CZ  TYR A 114      26.601  19.321  -5.178  1.00 39.49
A    C
ATOM    633  OH  TYR A 114      27.809  19.560  -5.789  1.00 40.81
A    O
ATOM    634  C   TYR A 114      21.069  16.810  -2.677  1.00 26.15
A    C
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ATOM    635  O   TYR A 114      20.987  16.549  -1.476  1.00 24.90
A    O
ATOM    636  N   MET A 115      20.006  16.906  -3.467  1.00 25.38
A    N
ATOM    637  CA  MET A 115      18.662  16.721  -2.948  1.00 24.05
A    C
ATOM    638  CB  MET A 115      17.646  16.865  -4.084  1.00 24.96
A    C
ATOM    639  CG  MET A 115      16.206  16.603  -3.708  1.00 24.12
A    C
ATOM    640  SD  MET A 115      15.563  17.820  -2.574  1.00 23.41
A    S
ATOM    641  CE  MET A 115      15.122  19.162  -3.708  1.00 23.60
A    C
ATOM    642  C   MET A 115      18.535  15.348  -2.300  1.00 24.70
A    C
ATOM    643  O   MET A 115      17.980  15.225  -1.218  1.00 22.93
A    O
ATOM    644  N   GLN A 116      19.085  14.327  -2.951  1.00 23.45
A    N
ATOM    645  CA  GLN A 116      19.005  12.962  -2.453  1.00 23.38
A    C
ATOM    646  CB  GLN A 116      19.439  12.001  -3.561  1.00 25.27
A    C
ATOM    647  CG  GLN A 116      18.491  12.034  -4.765  1.00 28.21
A    C
ATOM    648  CD  GLN A 116      18.550  13.344  -5.550  1.00 29.58
A    C
ATOM    649  OE1 GLN A 116      17.549  13.786  -6.116  1.00 32.33
A    O
ATOM    650  NE2 GLN A 116      19.727  13.956  -5.600  1.00 27.60
A    N
ATOM    651  C   GLN A 116      19.766  12.683  -1.160  1.00 21.18
A    C
ATOM    652  O   GLN A 116      19.570  11.650  -0.527  1.00 21.75
A    O
ATOM    653  N   GLU A 117      20.632  13.603  -0.761  1.00 19.23
A    N
ATOM    654  CA  GLU A 117      21.383  13.426   0.472  1.00 18.78
A    C
ATOM    655  CB  GLU A 117      22.834  13.851   0.272  1.00 22.01
A    C
ATOM    656  CG  GLU A 117      23.574  13.015  -0.751  1.00 26.21
A    C
ATOM    657  CD  GLU A 117      25.011  13.446  -0.915  1.00 28.09
A    C
ATOM    658  OE1 GLU A 117      25.245  14.584  -1.373  1.00 31.04
A    O
ATOM    659  OE2 GLU A 117      25.907  12.643  -0.583  1.00 29.29
A    O
ATOM    660  C   GLU A 117      20.765  14.252   1.592  1.00 15.64
A    C
ATOM    661  O   GLU A 117      20.748  13.834   2.742  1.00 12.05
A    O
ATOM    662  N   VAL A 118      20.247  15.423   1.233  1.00 12.54
A    N
ATOM    663  CA  VAL A 118      19.643  16.340   2.190  1.00 10.94
A    C
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ATOM    664  CB  VAL A 118      19.521  17.752   1.571  1.00 13.38
A    C
ATOM    665  CG1 VAL A 118      18.818  18.689   2.529  1.00 11.25
A    C
ATOM    666  CG2 VAL A 118      20.913  18.285   1.227  1.00 11.27
A    C
ATOM    667  C   VAL A 118      18.266  15.887   2.686  1.00 12.41
A    C
ATOM    668  O   VAL A 118      17.971  15.999   3.872  1.00 12.25
A    O
ATOM    669  N   VAL A 119      17.427  15.372   1.793  1.00 11.42
A    N
ATOM    670  CA  VAL A 119      16.097  14.942   2.208  1.00 13.06
A    C
ATOM    671  CB  VAL A 119      15.275  14.419   1.007  1.00 14.89
A    C
ATOM    672  CG1 VAL A 119      14.001  13.738   1.495  1.00 13.96
A    C
ATOM    673  CG2 VAL A 119      14.937  15.586   0.072  1.00 12.52
A    C
ATOM    674  C   VAL A 119      16.123  13.902   3.337  1.00 12.86
A    C
ATOM    675  O   VAL A 119      15.425  14.069   4.335  1.00 13.99
A    O
ATOM    676  N   PRO A 120      16.933  12.832   3.208  1.00 13.22
A    N
ATOM    677  CD  PRO A 120      17.731  12.385   2.052  1.00 13.49
A    C
ATOM    678  CA  PRO A 120      16.979  11.825   4.274  1.00 13.95
A    C
ATOM    679  CB  PRO A 120      17.979  10.798   3.743  1.00 13.50
A    C
ATOM    680  CG  PRO A 120      17.776  10.882   2.264  1.00 16.77
A    C
ATOM    681  C   PRO A 120      17.427  12.439   5.590  1.00 13.93
A    C
ATOM    682  O   PRO A 120      16.951  12.058   6.652  1.00 13.50
A    O
ATOM    683  N   PHE A 121      18.357  13.385   5.508  1.00 11.40
A    N
ATOM    684  CA  PHE A 121      18.860  14.078   6.692  1.00 11.01
A    C
ATOM    685  CB  PHE A 121      19.978  15.048   6.270  1.00 10.39
A    C
ATOM    686  CG  PHE A 121      20.327  16.085   7.309  1.00 12.29
A    C
ATOM    687  CD1 PHE A 121      20.796  15.713   8.561  1.00 10.86
A    C
ATOM    688  CD2 PHE A 121      20.220  17.440   7.011  1.00 12.84
A    C
ATOM    689  CE1 PHE A 121      21.153  16.678   9.506  1.00 11.52
A    C
ATOM    690  CE2 PHE A 121      20.573  18.416   7.951  1.00 13.64
A    C
ATOM    691  CZ  PHE A 121      21.042  18.034   9.195  1.00 11.27
A    C
ATOM    692  C   PHE A 121      17.715  14.837   7.383  1.00  9.92
A    C
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ATOM	693	O	PHE	A	121	17.474	14.658	8.575	1.00	10.41	A	O
ATOM	694	N	LEU	A	122	17.003	15.673	6.631	1.00	8.04	A	N
ATOM	695	CA	LEU	A	122	15.895	16.445	7.202	1.00	9.54	A	C
ATOM	696	CB	LEU	A	122	15.364	17.439	6.167	1.00	9.32	A	C
ATOM	697	CG	LEU	A	122	16.417	18.482	5.780	1.00	10.24	A	C
ATOM	698	CD1	LEU	A	122	15.888	19.366	4.658	1.00	12.89	A	C
ATOM	699	CD2	LEU	A	122	16.779	19.325	6.997	1.00	10.42	A	C
ATOM	700	C	LEU	A	122	14.765	15.551	7.714	1.00	9.19	A	C
ATOM	701	O	LEU	A	122	14.133	15.853	8.729	1.00	11.17	A	O
ATOM	702	N	ALA	A	123	14.508	14.454	7.012	1.00	10.07	A	N
ATOM	703	CA	ALA	A	123	13.473	13.518	7.432	1.00	11.76	A	C
ATOM	704	CB	ALA	A	123	13.307	12.415	6.385	1.00	11.58	A	C
ATOM	705	C	ALA	A	123	13.844	12.901	8.785	1.00	12.42	A	C
ATOM	706	O	ALA	A	123	12.972	12.651	9.629	1.00	10.87	A	O
ATOM	707	N	ARG	A	124	15.129	12.637	8.996	1.00	13.52	A	N
ATOM	708	CA	ARG	A	124	15.537	12.057	10.268	1.00	15.12	A	C
ATOM	709	CB	ARG	A	124	16.998	11.599	10.230	1.00	16.39	A	C
ATOM	710	CG	ARG	A	124	17.222	10.361	9.361	1.00	18.81	A	C
ATOM	711	CD	ARG	A	124	18.514	9.644	9.730	1.00	19.88	A	C
ATOM	712	NE	ARG	A	124	19.684	10.503	9.592	1.00	21.22	A	N
ATOM	713	CZ	ARG	A	124	20.241	10.818	8.429	1.00	21.14	A	C
ATOM	714	NH1	ARG	A	124	19.739	10.339	7.300	1.00	21.19	A	N
ATOM	715	NH2	ARG	A	124	21.292	11.620	8.398	1.00	21.84	A	N
ATOM	716	C	ARG	A	124	15.319	13.052	11.396	1.00	14.67	A	C
ATOM	717	O	ARG	A	124	14.968	12.666	12.509	1.00	14.02	A	O
ATOM	718	N	LEU	A	125	15.512	14.336	11.113	1.00	12.38	A	N
ATOM	719	CA	LEU	A	125	15.305	15.348	12.142	1.00	12.66	A	C
ATOM	720	CB	LEU	A	125	15.757	16.724	11.655	1.00	11.19	A	C
ATOM	721	CG	LEU	A	125	17.257	16.863	11.400	1.00	12.07	A	C

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ATOM    722  CD1 LEU A 125      17.571  18.262  10.880  1.00 11.21
A    C
ATOM    723  CD2 LEU A 125      18.015  16.567  12.691  1.00 10.90
A    C
ATOM    724  C   LEU A 125      13.824  15.384  12.457  1.00 12.64
A    C
ATOM    725  O   LEU A 125      13.424  15.502  13.615  1.00 13.64
A    O
ATOM    726  N   SER A 126      13.010  15.289  11.412  1.00 11.87
A    N
ATOM    727  CA  SER A 126      11.567  15.301  11.584  1.00 12.10
A    C
ATOM    728  CB  SER A 126      10.869  15.199  10.219  1.00 12.32
A    C
ATOM    729  OG  SER A 126       9.511  14.794  10.350  1.00 12.93
A    O
ATOM    730  C   SER A 126      11.174  14.124  12.466  1.00 14.19
A    C
ATOM    731  O   SER A 126      10.379  14.267  13.397  1.00 14.24
A    O
ATOM    732  N   ASN A 127      11.751  12.960  12.182  1.00 15.34
A    N
ATOM    733  CA  ASN A 127      11.441  11.761  12.953  1.00 19.77
A    C
ATOM    734  CB  ASN A 127      12.143  10.532  12.363  1.00 22.15
A    C
ATOM    735  CG  ASN A 127      11.687   9.236  13.020  1.00 27.13
A    C
ATOM    736  OD1 ASN A 127      10.492   8.925  13.039  1.00 29.33
A    O
ATOM    737  ND2 ASN A 127      12.634   8.479  13.564  1.00 27.25
A    N
ATOM    738  C   ASN A 127      11.839  11.922  14.416  1.00 19.60
A    C
ATOM    739  O   ASN A 127      11.162  11.412  15.305  1.00 19.90
A    O
ATOM    740  N   ARG A 128      12.934  12.629  14.672  1.00 19.27
A    N
ATOM    741  CA  ARG A 128      13.396  12.855  16.043  1.00 20.04
A    C
ATOM    742  CB  ARG A 128      14.783  13.534  15.992  1.00 20.58
A    C
ATOM    743  CG  ARG A 128      15.659  13.507  17.262  1.00 24.13
A    C
ATOM    744  CD  ARG A 128      15.120  14.392  18.371  1.00 27.44
A    C
ATOM    745  NE  ARG A 128      16.165  14.909  19.249  1.00 27.58
A    N
ATOM    746  CZ  ARG A 128      15.991  15.179  20.539  1.00 29.81
A    C
ATOM    747  NH1 ARG A 128      14.809  14.970  21.107  1.00 29.81
A    N
ATOM    748  NH2 ARG A 128      16.991  15.671  21.256  1.00 27.09
A    N
ATOM    749  C   ARG A 128      12.373  13.743  16.788  1.00 20.54
A    C
ATOM    750  O   ARG A 128      12.069  13.519  17.967  1.00 18.67
A    O
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ATOM    751  N   LEU A 129      11.850  14.753  16.098  1.00 19.98
A    N
ATOM    752  CA  LEU A 129      10.876  15.669  16.695  1.00 21.90
A    C
ATOM    753  CB  LEU A 129      10.813  16.965  15.886  1.00 19.92
A    C
ATOM    754  CG  LEU A 129      12.044  17.872  15.908  1.00 19.27
A    C
ATOM    755  CD1 LEU A 129      11.925  18.930  14.824  1.00 19.33
A    C
ATOM    756  CD2 LEU A 129      12.188  18.504  17.287  1.00 16.10
A    C
ATOM    757  C   LEU A 129       9.474  15.075  16.750  1.00 25.34
A    C
ATOM    758  O   LEU A 129       8.592  15.579  17.452  1.00 25.92
A    O
ATOM    759  N   SER A 130       9.270  14.007  15.994  1.00 28.06
A    N
ATOM    760  CA  SER A 130       7.969  13.364  15.910  1.00 33.42
A    C
ATOM    761  CB  SER A 130       8.095  11.979  15.288  1.00 32.53
A    C
ATOM    762  OG  SER A 130       8.750  11.096  16.177  1.00 35.12
A    O
ATOM    763  C   SER A 130       7.200  13.233  17.210  1.00 36.11
A    C
ATOM    764  O   SER A 130       7.681  12.658  18.190  1.00 38.33
A    O
ATOM    765  N   THR A 131       5.993  13.785  17.200  1.00 39.23
A    N
ATOM    766  CA  THR A 131       5.098  13.700  18.340  1.00 42.38
A    C
ATOM    767  CB  THR A 131       4.968  12.214  18.733  1.00 44.32
A    C
ATOM    768  OG1 THR A 131       4.843  11.445  17.527  1.00 47.57
A    O
ATOM    769  CG2 THR A 131       3.725  11.944  19.561  1.00 45.19
A    C
ATOM    770  C   THR A 131       5.448  14.576  19.558  1.00 42.64
A    C
ATOM    771  O   THR A 131       4.710  14.560  20.551  1.00 43.84
A    O
ATOM    772  N   CYS A 132       6.559  15.325  19.496  1.00 41.52
A    N
ATOM    773  CA  CYS A 132       6.930  16.219  20.603  1.00 39.84
A    C
ATOM    774  C   CYS A 132       5.899  17.299  20.541  1.00 40.10
A    C
ATOM    775  O   CYS A 132       5.358  17.570  19.471  1.00 40.22
A    O
ATOM    776  CB  CYS A 132       8.309  16.869  20.413  1.00 36.93
A    C
ATOM    777  SG  CYS A 132       8.480  18.000  18.999  1.00 32.53
A    S
ATOM    778  N   HIS A 133       5.624  17.927  21.673  1.00 40.74
A    N
ATOM    779  CA  HIS A 133       4.629  18.979  21.689  1.00 41.87
A    C
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ATOM    780  CB  HIS A 133       3.251  18.373  21.933  1.00 44.51
A    C
ATOM    781  CG  HIS A 133       3.122  17.694  23.260  1.00 47.49
A    C
ATOM    782  CD2 HIS A 133       2.913  16.396  23.583  1.00 48.42
A    C
ATOM    783  ND1 HIS A 133       3.241  18.371  24.455  1.00 48.25
A    N
ATOM    784  CE1 HIS A 133       3.114  17.518  25.457  1.00 48.41
A    C
ATOM    785  NE2 HIS A 133       2.915  16.313  24.955  1.00 48.80
A    N
ATOM    786  C   HIS A 133       4.916  20.023  22.750  1.00 41.49
A    C
ATOM    787  O   HIS A 133       5.897  19.924  23.488  1.00 40.33
A    O
ATOM    788  N   ILE A 134       4.050  21.030  22.811  1.00 41.32
A    N
ATOM    789  CA  ILE A 134       4.176  22.099  23.794  1.00 42.67
A    C
ATOM    790  CB  ILE A 134       4.176  23.493  23.120  1.00 42.74
A    C
ATOM    791  CG2 ILE A 134       5.446  23.663  22.301  1.00 42.04
A    C
ATOM    792  CG1 ILE A 134       2.918  23.649  22.255  1.00 41.70
A    C
ATOM    793  CD  ILE A 134       2.780  24.957  21.499  1.00 41.81
A    C
ATOM    794  C   ILE A 134       3.000  21.999  24.763  1.00 43.64
A    C
ATOM    795  O   ILE A 134       1.906  21.571  24.387  1.00 43.52
A    O
ATOM    796  N   GLU A 135       3.229  22.391  26.011  1.00 44.33
A    N
ATOM    797  CA  GLU A 135       2.189  22.319  27.031  1.00 45.59
A    C
ATOM    798  CB  GLU A 135       2.832  22.272  28.431  1.00 47.61
A    C
ATOM    799  CG  GLU A 135       3.765  23.448  28.742  1.00 50.52
A    C
ATOM    800  CD  GLU A 135       4.589  23.260  30.002  1.00 51.87
A    C
ATOM    801  OE1 GLU A 135       5.538  22.454  29.942  1.00 51.72
A    O
ATOM    802  OE2 GLU A 135       4.301  23.912  31.037  1.00 52.55
A    O
ATOM    803  C   GLU A 135       1.191  23.474  26.938  1.00 45.27
A    C
ATOM    804  O   GLU A 135       0.204  23.512  27.674  1.00 45.54
A    O
ATOM    805  N   GLY A 136       1.447  24.415  26.033  1.00 44.63
A    N
ATOM    806  CA  GLY A 136       0.557  25.553  25.878  1.00 43.02
A    C
ATOM    807  C   GLY A 136      -0.268  25.466  24.612  1.00 42.19
A    C
ATOM    808  O   GLY A 136      -0.205  24.469  23.894  1.00 42.03
A    O
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ATOM    809  N   ASP A 137      -1.048  26.507  24.341  1.00 41.98
A    N
ATOM    810  CA  ASP A 137      -1.881  26.544  23.146  1.00 41.03
A    C
ATOM    811  CB  ASP A 137      -2.996  27.576  23.310  1.00 43.41
A    C
ATOM    812  CG  ASP A 137      -3.844  27.710  22.064  1.00 45.06
A    C
ATOM    813  OD1 ASP A 137      -4.458  26.704  21.647  1.00 47.37
A    O
ATOM    814  OD2 ASP A 137      -3.892  28.821  21.499  1.00 45.71
A    O
ATOM    815  C   ASP A 137      -1.016  26.908  21.944  1.00 39.51
A    C
ATOM    816  O   ASP A 137      -0.162  27.783  22.036  1.00 39.46
A    O
ATOM    817  N   ASP A 138      -1.241  26.244  20.814  1.00 38.39
A    N
ATOM    818  CA  ASP A 138      -0.439  26.511  19.621  1.00 37.99
A    C
ATOM    819  CB  ASP A 138       0.168  25.208  19.102  1.00 39.01
A    C
ATOM    820  CG  ASP A 138      -0.874  24.264  18.548  1.00 39.32
A    C
ATOM    821  OD1 ASP A 138      -2.070  24.475  18.826  1.00 39.65
A    O
ATOM    822  OD2 ASP A 138      -0.500  23.307  17.842  1.00 41.75
A    O
ATOM    823  C   ASP A 138      -1.219  27.186  18.501  1.00 36.81
A    C
ATOM    824  O   ASP A 138      -0.832  27.116  17.335  1.00 35.87
A    O
ATOM    825  N   LEU A 139      -2.315  27.849  18.857  1.00 34.57
A    N
ATOM    826  CA  LEU A 139      -3.139  28.532  17.870  1.00 33.64
A    C
ATOM    827  CB  LEU A 139      -4.321  29.219  18.563  1.00 34.78
A    C
ATOM    828  CG  LEU A 139      -5.618  29.352  17.757  1.00 36.95
A    C
ATOM    829  CD1 LEU A 139      -6.663  30.071  18.602  1.00 36.17
A    C
ATOM    830  CD2 LEU A 139      -5.364  30.112  16.464  1.00 36.43
A    C
ATOM    831  C   LEU A 139      -2.326  29.561  17.079  1.00 31.14
A    C
ATOM    832  O   LEU A 139      -2.461  29.666  15.862  1.00 30.79
A    O
ATOM    833  N   HIS A 140      -1.483  30.318  17.769  1.00 29.61
A    N
ATOM    834  CA  HIS A 140      -0.671  31.329  17.103  1.00 29.77
A    C
ATOM    835  CB  HIS A 140       0.039  32.210  18.138  1.00 32.63
A    C
ATOM    836  CG  HIS A 140       0.926  31.453  19.078  1.00 35.82
A    C
ATOM    837  CD2 HIS A 140       2.183  31.706  19.515  1.00 36.65
A    C
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ATOM    838  ND1 HIS A 140       0.524  30.297  19.713  1.00 37.28
A    N
ATOM    839  CE1 HIS A 140       1.496  29.870  20.500  1.00 38.18
A    C
ATOM    840  NE2 HIS A 140       2.514  30.707  20.399  1.00 36.65
A    N
ATOM    841  C   HIS A 140       0.342  30.664  16.180  1.00 28.45
A    C
ATOM    842  O   HIS A 140       0.639  31.171  15.102  1.00 28.05
A    O
ATOM    843  N   ILE A 141       0.857  29.514  16.597  1.00 27.82
A    N
ATOM    844  CA  ILE A 141       1.825  28.784  15.790  1.00 26.79
A    C
ATOM    845  CB  ILE A 141       2.424  27.616  16.595  1.00 26.52
A    C
ATOM    846  CG2 ILE A 141       3.057  26.598  15.667  1.00 24.81
A    C
ATOM    847  CG1 ILE A 141       3.434  28.174  17.605  1.00 26.50
A    C
ATOM    848  CD  ILE A 141       3.981  27.146  18.563  1.00 28.45
A    C
ATOM    849  C   ILE A 141       1.168  28.269  14.516  1.00 27.29
A    C
ATOM    850  O   ILE A 141       1.749  28.344  13.434  1.00 26.99
A    O
ATOM    851  N   GLN A 142      -0.053  27.760  14.647  1.00 28.53
A    N
ATOM    852  CA  GLN A 142      -0.788  27.249  13.497  1.00 27.65
A    C
ATOM    853  CB  GLN A 142      -2.128  26.667  13.940  1.00 29.20
A    C
ATOM    854  CG  GLN A 142      -2.026  25.340  14.674  1.00 32.99
A    C
ATOM    855  CD  GLN A 142      -3.388  24.786  15.049  1.00 35.51
A    C
ATOM    856  OE1 GLN A 142      -4.111  25.378  15.850  1.00 40.18
A    O
ATOM    857  NE2 GLN A 142      -3.748  23.651  14.464  1.00 36.87
A    N
ATOM    858  C   GLN A 142      -1.025  28.354  12.473  1.00 26.74
A    C
ATOM    859  O   GLN A 142      -0.895  28.132  11.272  1.00 26.24
A    O
ATOM    860  N   ARG A 143      -1.376  29.542  12.953  1.00 27.29
A    N
ATOM    861  CA  ARG A 143      -1.622  30.679  12.071  1.00 27.82
A    C
ATOM    862  CB  ARG A 143      -2.106  31.886  12.878  1.00 29.63
A    C
ATOM    863  CG  ARG A 143      -3.526  31.758  13.405  1.00 34.47
A    C
ATOM    864  CD  ARG A 143      -3.788  32.781  14.507  1.00 39.86
A    C
ATOM    865  NE  ARG A 143      -5.170  32.741  14.977  1.00 44.13
A    N
ATOM    866  CZ  ARG A 143      -5.575  33.213  16.152  1.00 46.89
A    C
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ATOM    867  NH1 ARG A 143      -4.701  33.762  16.987  1.00 47.65
A    N
ATOM    868  NH2 ARG A 143      -6.856  33.132  16.493  1.00 48.27
A    N
ATOM    869  C   ARG A 143      -0.363  31.064  11.301  1.00 26.24
A    C
ATOM    870  O   ARG A 143      -0.410  31.289  10.094  1.00 24.10
A    O
ATOM    871  N   ASN A 144       0.761  31.136  12.004  1.00 25.57
A    N
ATOM    872  CA  ASN A 144       2.024  31.511  11.377  1.00 25.34
A    C
ATOM    873  CB  ASN A 144       3.113  31.670  12.442  1.00 25.23
A    C
ATOM    874  CG  ASN A 144       2.901  32.901  13.310  1.00 27.47
A    C
ATOM    875  OD1 ASN A 144       1.855  33.552  13.238  1.00 25.19
A    O
ATOM    876  ND2 ASN A 144       3.894  33.225  14.137  1.00 26.15
A    N
ATOM    877  C   ASN A 144       2.460  30.508  10.319  1.00 24.78
A    C
ATOM    878  O   ASN A 144       2.963  30.896   9.259  1.00 24.90
A    O
ATOM    879  N   VAL A 145       2.262  29.222  10.599  1.00 23.95
A    N
ATOM    880  CA  VAL A 145       2.638  28.177   9.650  1.00 22.12
A    C
ATOM    881  CB  VAL A 145       2.578  26.771  10.298  1.00 22.24
A    C
ATOM    882  CG1 VAL A 145       2.893  25.703   9.265  1.00 22.51
A    C
ATOM    883  CG2 VAL A 145       3.571  26.688  11.442  1.00 19.36
A    C
ATOM    884  C   VAL A 145       1.705  28.219   8.445  1.00 23.02
A    C
ATOM    885  O   VAL A 145       2.143  28.075   7.304  1.00 20.64
A    O
ATOM    886  N   GLN A 146       0.417  28.430   8.703  1.00 24.15
A    N
ATOM    887  CA  GLN A 146      -0.566  28.491   7.630  1.00 23.03
A    C
ATOM    888  CB  GLN A 146      -1.962  28.746   8.197  1.00 25.85
A    C
ATOM    889  CG  GLN A 146      -3.056  28.631   7.153  1.00 27.55
A    C
ATOM    890  CD  GLN A 146      -3.028  27.291   6.443  1.00 27.72
A    C
ATOM    891  OE1 GLN A 146      -2.920  27.228   5.221  1.00 28.53
A    O
ATOM    892  NE2 GLN A 146      -3.125  26.210   7.210  1.00 29.98
A    N
ATOM    893  C   GLN A 146      -0.227  29.586   6.625  1.00 23.12
A    C
ATOM    894  O   GLN A 146      -0.409  29.411   5.422  1.00 22.07
A    O
ATOM    895  N   LYS A 147       0.253  30.720   7.120  1.00 21.60
A    N
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ATOM    896  CA  LYS A 147       0.609  31.826   6.242  1.00 23.99
A    C
ATOM    897  CB  LYS A 147       0.982  33.069   7.054  1.00 27.26
A    C
ATOM    898  CG  LYS A 147       1.356  34.266   6.183  1.00 33.40
A    C
ATOM    899  CD  LYS A 147       0.223  34.614   5.211  1.00 37.04
A    C
ATOM    900  CE  LYS A 147       0.599  35.760   4.278  1.00 38.65
A    C
ATOM    901  NZ  LYS A 147       0.882  37.019   5.027  1.00 40.65
A    N
ATOM    902  C   LYS A 147       1.778  31.441   5.349  1.00 24.34
A    C
ATOM    903  O   LYS A 147       1.860  31.861   4.193  1.00 21.81
A    O
ATOM    904  N   LEU A 148       2.696  30.650   5.894  1.00 23.83
A    N
ATOM    905  CA  LEU A 148       3.844  30.216   5.120  1.00 23.73
A    C
ATOM    906  CB  LEU A 148       4.864  29.516   6.029  1.00 24.60
A    C
ATOM    907  CG  LEU A 148       6.213  29.108   5.425  1.00 25.23
A    C
ATOM    908  CD1 LEU A 148       7.213  28.802   6.539  1.00 27.40
A    C
ATOM    909  CD2 LEU A 148       6.023  27.897   4.535  1.00 25.60
A    C
ATOM    910  C   LEU A 148       3.315  29.272   4.043  1.00 21.03
A    C
ATOM    911  O   LEU A 148       3.706  29.364   2.885  1.00 22.18
A    O
ATOM    912  N   LYS A 149       2.411  28.376   4.422  1.00 21.82
A    N
ATOM    913  CA  LYS A 149       1.834  27.439   3.461  1.00 22.95
A    C
ATOM    914  CB  LYS A 149       0.852  26.495   4.148  1.00 24.40
A    C
ATOM    915  CG  LYS A 149       1.462  25.605   5.209  1.00 26.03
A    C
ATOM    916  CD  LYS A 149       0.433  24.591   5.683  1.00 29.36
A    C
ATOM    917  CE  LYS A 149       1.026  23.603   6.667  1.00 31.50
A    C
ATOM    918  NZ  LYS A 149       0.039  22.535   7.000  1.00 33.82
A    N
ATOM    919  C   LYS A 149       1.098  28.204   2.366  1.00 23.21
A    C
ATOM    920  O   LYS A 149       1.239  27.899   1.177  1.00 21.94
A    O
ATOM    921  N   ASP A 150       0.319  29.203   2.771  1.00 22.28
A    N
ATOM    922  CA  ASP A 150      -0.441  30.003   1.814  1.00 23.20
A    C
ATOM    923  CB  ASP A 150      -1.303  31.054   2.526  1.00 25.06
A    C
ATOM    924  CG  ASP A 150      -2.359  30.444   3.430  1.00 27.96
A    C
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ATOM    925  OD1 ASP A 150      -2.832  29.327   3.140  1.00 29.25
A    O
ATOM    926  OD2 ASP A 150      -2.731  31.100   4.428  1.00 30.84
A    O
ATOM    927  C   ASP A 150       0.487  30.716   0.844  1.00 22.09
A    C
ATOM    928  O   ASP A 150       0.201  30.804  -0.349  1.00 22.07
A    O
ATOM    929  N   THR A 151       1.599  31.228   1.360  1.00 20.13
A    N
ATOM    930  CA  THR A 151       2.557  31.949   0.533  1.00 20.21
A    C
ATOM    931  CB  THR A 151       3.676  32.578   1.390  1.00 21.32
A    C
ATOM    932  OG1 THR A 151       3.097  33.422   2.392  1.00 22.82
A    O
ATOM    933  CG2 THR A 151       4.602  33.410   0.520  1.00 23.30
A    C
ATOM    934  C   THR A 151       3.184  31.045  -0.521  1.00 19.34
A    C
ATOM    935  O   THR A 151       3.403  31.466  -1.659  1.00 16.62
A    O
ATOM    936  N   VAL A 152       3.482  29.809  -0.134  1.00 17.83
A    N
ATOM    937  CA  VAL A 152       4.071  28.849  -1.056  1.00 20.82
A    C
ATOM    938  CB  VAL A 152       4.465  27.545  -0.322  1.00 19.02
A    C
ATOM    939  CG1 VAL A 152       4.739  26.433  -1.323  1.00 21.92
A    C
ATOM    940  CG2 VAL A 152       5.716  27.782   0.507  1.00 20.80
A    C
ATOM    941  C   VAL A 152       3.087  28.535  -2.183  1.00 22.16
A    C
ATOM    942  O   VAL A 152       3.479  28.449  -3.346  1.00 23.43
A    O
ATOM    943  N   LYS A 153       1.810  28.379  -1.843  1.00 24.38
A    N
ATOM    944  CA  LYS A 153       0.789  28.087  -2.849  1.00 27.82
A    C
ATOM    945  CB  LYS A 153      -0.534  27.732  -2.176  1.00 31.58
A    C
ATOM    946  CG  LYS A 153      -0.441  26.583  -1.209  1.00 35.04
A    C
ATOM    947  CD  LYS A 153      -1.778  26.401  -0.548  1.00 40.47
A    C
ATOM    948  CE  LYS A 153      -1.689  25.379   0.560  1.00 43.02
A    C
ATOM    949  NZ  LYS A 153      -2.952  25.190   1.344  1.00 44.36
A    N
ATOM    950  C   LYS A 153       0.585  29.279  -3.784  1.00 29.16
A    C
ATOM    951  O   LYS A 153       0.437  29.108  -4.996  1.00 28.68
A    O
ATOM    952  N   LYS A 154       0.580  30.484  -3.218  1.00 28.50
A    N
ATOM    953  CA  LYS A 154       0.402  31.699  -4.005  1.00 29.69
A    C
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ATOM    954  CB  LYS A 154       0.479  32.942  -3.106  1.00 32.52
A    C
ATOM    955  CG  LYS A 154      -0.616  33.048  -2.053  1.00 37.41
A    C
ATOM    956  CD  LYS A 154      -0.339  34.206  -1.095  1.00 40.74
A    C
ATOM    957  CE  LYS A 154      -1.385  34.290   0.009  1.00 42.32
A    C
ATOM    958  NZ  LYS A 154      -1.038  35.319   1.032  1.00 42.89
A    N
ATOM    959  C   LYS A 154       1.496  31.788  -5.064  1.00 28.78
A    C
ATOM    960  O   LYS A 154       1.291  32.351  -6.144  1.00 28.74
A    O
ATOM    961  N   LEU A 155       2.661  31.232  -4.738  1.00 26.21
A    N
ATOM    962  CA  LEU A 155       3.805  31.253  -5.640  1.00 24.24
A    C
ATOM    963  CB  LEU A 155       5.118  31.313  -4.847  1.00 22.63
A    C
ATOM    964  CG  LEU A 155       5.392  32.561  -3.979  1.00 24.03
A    C
ATOM    965  CD1 LEU A 155       6.695  32.374  -3.263  1.00 25.32
A    C
ATOM    966  CD2 LEU A 155       5.518  33.828  -4.793  1.00 23.74
A    C
ATOM    967  C   LEU A 155       3.807  30.058  -6.576  1.00 22.47
A    C
ATOM    968  O   LEU A 155       4.504  30.059  -7.590  1.00 22.33
A    O
ATOM    969  N   GLY A 156       3.009  29.051  -6.240  1.00 23.16
A    N
ATOM    970  CA  GLY A 156       2.927  27.864  -7.068  1.00 22.02
A    C
ATOM    971  C   GLY A 156       4.208  27.063  -7.063  1.00 21.25
A    C
ATOM    972  O   GLY A 156       4.829  26.876  -6.020  1.00 21.24
A    O
ATOM    973  N   GLU A 157       4.604  26.585  -8.236  1.00 20.06
A    N
ATOM    974  CA  GLU A 157       5.816  25.788  -8.371  1.00 21.41
A    C
ATOM    975  CB  GLU A 157       6.055  25.449  -9.849  1.00 23.31
A    C
ATOM    976  CG  GLU A 157       7.319  24.650 -10.107  1.00 28.64
A    C
ATOM    977  CD  GLU A 157       7.147  23.189  -9.770  1.00 31.67
A    C
ATOM    978  OE1 GLU A 157       6.397  22.891  -8.824  1.00 34.33
A    O
ATOM    979  OE2 GLU A 157       7.765  22.334 -10.439  1.00 33.96
A    O
ATOM    980  C   GLU A 157       7.029  26.539  -7.817  1.00 19.72
A    C
ATOM    981  O   GLU A 157       7.860  25.971  -7.105  1.00 19.07
A    O
ATOM    982  N   SER A 158       7.129  27.821  -8.147  1.00 18.69
A    N
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ATOM    983  CA  SER A 158       8.249  28.624  -7.680  1.00 19.07
A    C
ATOM    984  CB  SER A 158       8.218  30.006  -8.337  1.00 20.27
A    C
ATOM    985  OG  SER A 158       7.058  30.717  -7.957  1.00 24.37
A    O
ATOM    986  C   SER A 158       8.225  28.761  -6.158  1.00 17.90
A    C
ATOM    987  O   SER A 158       9.214  29.166  -5.549  1.00 16.77
A    O
ATOM    988  N   GLY A 159       7.088  28.433  -5.552  1.00 15.07
A    N
ATOM    989  CA  GLY A 159       6.975  28.500  -4.108  1.00 13.85
A    C
ATOM    990  C   GLY A 159       7.806  27.375  -3.524  1.00 12.96
A    C
ATOM    991  O   GLY A 159       8.496  27.545  -2.521  1.00 11.66
A    O
ATOM    992  N   GLU A 160       7.729  26.215  -4.163  1.00 13.13
A    N
ATOM    993  CA  GLU A 160       8.486  25.046  -3.741  1.00 14.60
A    C
ATOM    994  CB  GLU A 160       8.017  23.820  -4.522  1.00 16.03
A    C
ATOM    995  CG  GLU A 160       6.665  23.291  -4.073  1.00 17.68
A    C
ATOM    996  CD  GLU A 160       6.076  22.326  -5.082  1.00 19.55
A    C
ATOM    997  OE1 GLU A 160       6.849  21.556  -5.687  1.00 19.93
A    O
ATOM    998  OE2 GLU A 160       4.843  22.341  -5.266  1.00 24.36
A    O
ATOM    999  C   GLU A 160       9.972  25.293  -3.988  1.00 13.84
A    C
ATOM   1000  O   GLU A 160      10.819  24.908  -3.180  1.00 13.51
A    O
ATOM   1001  N   ILE A 161      10.278  25.941  -5.109  1.00 13.97
A    N
ATOM   1002  CA  ILE A 161      11.659  26.262  -5.457  1.00 15.01
A    C
ATOM   1003  CB  ILE A 161      11.752  26.949  -6.853  1.00 16.72
A    C
ATOM   1004  CG2 ILE A 161      13.191  27.359  -7.146  1.00 15.56
A    C
ATOM   1005  CG1 ILE A 161      11.225  26.012  -7.947  1.00 16.62
A    C
ATOM   1006  CD  ILE A 161      11.853  24.641  -7.954  1.00 19.54
A    C
ATOM   1007  C   ILE A 161      12.220  27.219  -4.399  1.00 14.73
A    C
ATOM   1008  O   ILE A 161      13.351  27.053  -3.927  1.00 15.29
A    O
ATOM   1009  N   LYS A 162      11.424  28.216  -4.024  1.00 11.62
A    N
ATOM   1010  CA  LYS A 162      11.852  29.185  -3.021  1.00 12.12
A    C
ATOM   1011  CB  LYS A 162      10.787  30.269  -2.829  1.00 12.70
A    C
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ATOM   1012  CG  LYS A 162      11.098  31.245  -1.697  1.00 11.50
A    C
ATOM   1013  CD  LYS A 162      10.128  32.416  -1.676  1.00 15.16
A    C
ATOM   1014  CE  LYS A 162      10.361  33.352  -2.853  1.00 15.54
A    C
ATOM   1015  NZ  LYS A 162      11.753  33.881  -2.894  1.00 17.14
A    N
ATOM   1016  C   LYS A 162      12.146  28.503  -1.686  1.00 13.23
A    C
ATOM   1017  O   LYS A 162      13.160  28.792  -1.050  1.00 13.30
A    O
ATOM   1018  N   ALA A 163      11.260  27.603  -1.266  1.00 12.38
A    N
ATOM   1019  CA  ALA A 163      11.438  26.880  -0.009  1.00 12.47
A    C
ATOM   1020  CB  ALA A 163      10.286  25.913   0.211  1.00 12.98
A    C
ATOM   1021  C   ALA A 163      12.756  26.117  -0.011  1.00 13.14
A    C
ATOM   1022  O   ALA A 163      13.452  26.062   1.008  1.00 12.48
A    O
ATOM   1023  N   ILE A 164      13.095  25.516  -1.149  1.00 12.42
A    N
ATOM   1024  CA  ILE A 164      14.346  24.780  -1.260  1.00 11.86
A    C
ATOM   1025  CB  ILE A 164      14.435  23.993  -2.589  1.00 12.07
A    C
ATOM   1026  CG2 ILE A 164      15.731  23.202  -2.635  1.00 10.78
A    C
ATOM   1027  CG1 ILE A 164      13.262  23.017  -2.718  1.00 12.17
A    C
ATOM   1028  CD  ILE A 164      13.278  22.229  -4.022  1.00 12.86
A    C
ATOM   1029  C   ILE A 164      15.491  25.800  -1.204  1.00 12.22
A    C
ATOM   1030  O   ILE A 164      16.541  25.545  -0.610  1.00 11.10
A    O
ATOM   1031  N   GLY A 165      15.281  26.955  -1.826  1.00 10.67
A    N
ATOM   1032  CA  GLY A 165      16.303  27.989  -1.813  1.00 12.02
A    C
ATOM   1033  C   GLY A 165      16.550  28.534  -0.417  1.00 13.62
A    C
ATOM   1034  O   GLY A 165      17.609  29.107  -0.140  1.00 12.29
A    O
ATOM   1035  N   GLU A 166      15.571  28.365   0.468  1.00 12.40
A    N
ATOM   1036  CA  GLU A 166      15.698  28.837   1.846  1.00 13.51
A    C
ATOM   1037  CB  GLU A 166      14.395  29.508   2.309  1.00 13.61
A    C
ATOM   1038  CG  GLU A 166      14.217  30.919   1.757  1.00 16.87
A    C
ATOM   1039  CD  GLU A 166      13.013  31.651   2.334  1.00 18.65
A    C
ATOM   1040  OE1 GLU A 166      12.660  31.392   3.504  1.00 15.68
A    O
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ATOM   1041  OE2 GLU A 166      12.435  32.507   1.618  1.00 18.26
A    O
ATOM   1042  C   GLU A 166      16.068  27.720   2.821  1.00 13.52
A    C
ATOM   1043  O   GLU A 166      15.908  27.877   4.028  1.00 12.78
A    O
ATOM   1044  N   LEU A 167      16.563  26.594   2.310  1.00 12.05
A    N
ATOM   1045  CA  LEU A 167      16.937  25.505   3.203  1.00 11.58
A    C
ATOM   1046  CB  LEU A 167      17.366  24.264   2.417  1.00 13.77
A    C
ATOM   1047  CG  LEU A 167      16.223  23.441   1.818  1.00 14.22
A    C
ATOM   1048  CD1 LEU A 167      16.778  22.130   1.246  1.00 16.24
A    C
ATOM   1049  CD2 LEU A 167      15.179  23.155   2.895  1.00 16.98
A    C
ATOM   1050  C   LEU A 167      18.048  25.922   4.158  1.00 12.19
A    C
ATOM   1051  O   LEU A 167      18.206  25.334   5.233  1.00 11.69
A    O
ATOM   1052  N   ASP A 168      18.816  26.937   3.770  1.00 12.76
A    N
ATOM   1053  CA  ASP A 168      19.887  27.419   4.625  1.00 13.15
A    C
ATOM   1054  CB  ASP A 168      20.843  28.342   3.848  1.00 16.25
A    C
ATOM   1055  CG  ASP A 168      20.139  29.497   3.160  1.00 19.91
A    C
ATOM   1056  OD1 ASP A 168      18.915  29.421   2.926  1.00 18.66
A    O
ATOM   1057  OD2 ASP A 168      20.827  30.487   2.832  1.00 20.94
A    O
ATOM   1058  C   ASP A 168      19.279  28.116   5.836  1.00 13.72
A    C
ATOM   1059  O   ASP A 168      19.777  27.975   6.953  1.00 15.78
A    O
ATOM   1060  N   LEU A 169      18.190  28.851   5.622  1.00 13.06
A    N
ATOM   1061  CA  LEU A 169      17.499  29.523   6.717  1.00 13.54
A    C
ATOM   1062  CB  LEU A 169      16.525  30.577   6.173  1.00 14.93
A    C
ATOM   1063  CG  LEU A 169      17.254  31.653   5.365  1.00 16.86
A    C
ATOM   1064  CD1 LEU A 169      16.306  32.688   4.873  1.00 17.37
A    C
ATOM   1065  CD2 LEU A 169      18.260  32.337   6.229  1.00 19.91
A    C
ATOM   1066  C   LEU A 169      16.738  28.499   7.556  1.00 12.68
A    C
ATOM   1067  O   LEU A 169      16.595  28.659   8.770  1.00 13.63
A    O
ATOM   1068  N   LEU A 170      16.251  27.446   6.905  1.00 12.87
A    N
ATOM   1069  CA  LEU A 170      15.526  26.397   7.604  1.00 12.73
A    C
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ATOM   1070  CB  LEU A 170      14.937  25.387   6.612  1.00 13.33
A    C
ATOM   1071  CG  LEU A 170      14.185  24.231   7.280  1.00 14.18
A    C
ATOM   1072  CD1 LEU A 170      13.048  24.789   8.111  1.00 15.94
A    C
ATOM   1073  CD2 LEU A 170      13.649  23.275   6.225  1.00 15.77
A    C
ATOM   1074  C   LEU A 170      16.514  25.677   8.506  1.00 11.78
A    C
ATOM   1075  O   LEU A 170      16.230  25.398   9.671  1.00 10.15
A    O
ATOM   1076  N   PHE A 171      17.676  25.371   7.947  1.00 12.13
A    N
ATOM   1077  CA  PHE A 171      18.716  24.684   8.690  1.00 11.64
A    C
ATOM   1078  CB  PHE A 171      19.938  24.478   7.787  1.00 12.34
A    C
ATOM   1079  CG  PHE A 171      21.100  23.800   8.465  1.00 13.38
A    C
ATOM   1080  CD1 PHE A 171      21.980  24.529   9.262  1.00 12.95
A    C
ATOM   1081  CD2 PHE A 171      21.330  22.438   8.282  1.00 12.74
A    C
ATOM   1082  CE1 PHE A 171      23.077  23.911   9.862  1.00 12.19
A    C
ATOM   1083  CE2 PHE A 171      22.426  21.808   8.878  1.00 13.42
A    C
ATOM   1084  CZ  PHE A 171      23.303  22.549   9.670  1.00  9.66
A    C
ATOM   1085  C   PHE A 171      19.097  25.487   9.933  1.00 12.85
A    C
ATOM   1086  O   PHE A 171      19.112  24.956  11.047  1.00 13.16
A    O
ATOM   1087  N   MET A 172      19.367  26.773   9.739  1.00 12.41
A    N
ATOM   1088  CA  MET A 172      19.770  27.633  10.845  1.00 13.98
A    C
ATOM   1089  CB AMET A 172      20.339  28.952  10.310  0.80 15.64
A    C
ATOM   1090  CB BMET A 172      20.370  28.959  10.355  0.20 14.94
A    C
ATOM   1091  CG AMET A 172      21.571  28.732   9.435  0.80 16.09
A    C
ATOM   1092  CG BMET A 172      19.527  29.804   9.448  0.20 15.64
A    C
ATOM   1093  SD AMET A 172      22.552  30.211   9.177  0.80 21.52
A    S
ATOM   1094  SD BMET A 172      20.472  31.295   9.068  0.20 14.45
A    S
ATOM   1095  CE AMET A 172      21.697  30.932   7.776  0.80 17.67
A    C
ATOM   1096  CE BMET A 172      21.541  30.699   7.752  0.20 18.36
A    C
ATOM   1097  C   MET A 172      18.662  27.902  11.848  1.00 13.07
A    C
ATOM   1098  O   MET A 172      18.937  28.048  13.039  1.00 13.04
A    O
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ATOM   1099  N   SER A 173      17.418  27.947  11.379  1.00 13.08
A    N
ATOM   1100  CA  SER A 173      16.284  28.199  12.261  1.00 11.55
A    C
ATOM   1101  CB  SER A 173      15.044  28.557  11.440  1.00 11.95
A    C
ATOM   1102  OG  SER A 173      15.174  29.828  10.818  1.00 14.62
A    O
ATOM   1103  C   SER A 173      16.019  26.963  13.127  1.00 11.91
A    C
ATOM   1104  O   SER A 173      15.713  27.082  14.315  1.00 14.96
A    O
ATOM   1105  N   LEU A 174      16.121  25.777  12.529  1.00 11.90
A    N
ATOM   1106  CA  LEU A 174      15.927  24.539  13.279  1.00 12.23
A    C
ATOM   1107  CB  LEU A 174      16.053  23.319  12.351  1.00 13.54
A    C
ATOM   1108  CG  LEU A 174      14.780  22.851  11.634  1.00 15.89
A    C
ATOM   1109  CD1 LEU A 174      15.132  21.898  10.491  1.00 14.93
A    C
ATOM   1110  CD2 LEU A 174      13.845  22.183  12.637  1.00 12.22
A    C
ATOM   1111  C   LEU A 174      16.999  24.465  14.371  1.00 12.75
A    C
ATOM   1112  O   LEU A 174      16.710  24.160  15.521  1.00 13.46
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ATOM   1113  N   ARG A 175      18.243  24.746  13.993  1.00 11.68
A    N
ATOM   1114  CA  ARG A 175      19.360  24.709  14.930  1.00 14.76
A    C
ATOM   1115  CB  ARG A 175      20.673  24.990  14.177  1.00 12.95
A    C
ATOM   1116  CG  ARG A 175      21.888  25.301  15.040  1.00 15.09
A    C
ATOM   1117  CD  ARG A 175      23.156  25.325  14.175  1.00 13.01
A    C
ATOM   1118  NE  ARG A 175      24.292  25.954  14.847  1.00 16.67
A    N
ATOM   1119  CZ  ARG A 175      25.566  25.771  14.505  1.00 15.77
A    C
ATOM   1120  NH1 ARG A 175      25.888  24.962  13.502  1.00 11.71
A    N
ATOM   1121  NH2 ARG A 175      26.525  26.429  15.144  1.00 16.45
A    N
ATOM   1122  C   ARG A 175      19.146  25.733  16.051  1.00 14.85
A    C
ATOM   1123  O   ARG A 175      19.163  25.392  17.235  1.00 16.14
A    O
ATOM   1124  N   ASN A 176      18.898  26.978  15.678  1.00 12.31
A    N
ATOM   1125  CA  ASN A 176      18.708  28.021  16.678  1.00 13.85
A    C
ATOM   1126  CB  ASN A 176      18.582  29.387  16.000  1.00 11.88
A    C
ATOM   1127  CG  ASN A 176      19.870  29.825  15.332  1.00 15.20
A    C
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ATOM   1128  OD1 ASN A 176      20.956  29.382  15.705  1.00 14.68
A    O
ATOM   1129  ND2 ASN A 176      19.759  30.709  14.350  1.00 13.94
A    N
ATOM   1130  C   ASN A 176      17.519  27.799  17.612  1.00 13.45
A    C
ATOM   1131  O   ASN A 176      17.609  28.060  18.812  1.00 13.27
A    O
ATOM   1132  N   ALA A 177      16.410  27.303  17.079  1.00 12.70
A    N
ATOM   1133  CA  ALA A 177      15.233  27.092  17.913  1.00 13.82
A    C
ATOM   1134  CB  ALA A 177      13.961  27.151  17.049  1.00 12.99
A    C
ATOM   1135  C   ALA A 177      15.240  25.793  18.701  1.00 13.69
A    C
ATOM   1136  O   ALA A 177      14.581  25.693  19.735  1.00 13.56
A    O
ATOM   1137  N   CYS A 178      16.013  24.808  18.255  1.00 12.34
A    N
ATOM   1138  CA  CYS A 178      15.954  23.505  18.917  1.00 12.68
A    C
ATOM   1139  C   CYS A 178      17.144  23.035  19.788  1.00 12.67
A    C
ATOM   1140  O   CYS A 178      16.965  22.126  20.591  1.00 12.42
A    O
ATOM   1141  CB  CYS A 178      15.703  22.419  17.872  1.00 12.70
A    C
ATOM   1142  SG  CYS A 178      14.143  22.611  16.953  1.00 13.36
A    S
ATOM   1143  N   ILE A 179      18.323  23.620  19.637  1.00 15.23
A    N
ATOM   1144  CA  ILE A 179      19.456  23.173  20.438  1.00 18.51
A    C
ATOM   1145  CB  ILE A 179      20.789  23.611  19.808  1.00 17.80
A    C
ATOM   1146  CG2 ILE A 179      20.887  23.039  18.390  1.00 15.56
A    C
ATOM   1147  CG1 ILE A 179      20.891  25.138  19.793  1.00 17.43
A    C
ATOM   1148  CD  ILE A 179      22.185  25.660  19.200  1.00 18.12
A    C
ATOM   1149  C   ILE A 179      19.384  23.657  21.886  1.00 22.43
A    C
ATOM   1150  OT1 ILE A 179      19.937  22.965  22.766  1.00 24.68
A    O
ATOM   1151  OT2 ILE A 179      18.783  24.728  22.123  1.00 25.46
A    O
ATOM   1152  CB  HIS B  39      27.892  44.470  -6.060  1.00 45.22
B    C
ATOM   1153  CG  HIS B  39      28.041  43.710  -7.341  1.00 48.50
B    C
ATOM   1154  CD2 HIS B  39      27.587  42.488  -7.704  1.00 50.10
B    C
ATOM   1155  ND1 HIS B  39      28.700  44.216  -8.442  1.00 50.41
B    N
ATOM   1156  CE1 HIS B  39      28.644  43.338  -9.428  1.00 50.37
B    C
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ATOM   1157  NE2 HIS B  39      27.974  42.281  -9.007  1.00 50.98
B    N
ATOM   1158  C   HIS B  39      29.987  43.757  -4.873  1.00 43.85
B    C
ATOM   1159  O   HIS B  39      31.015  43.319  -5.402  1.00 43.28
B    O
ATOM   1160  N   HIS B  39      29.995  45.653  -6.496  1.00 43.51
B    N
ATOM   1161  CA  HIS B  39      29.215  44.936  -5.463  1.00 44.10
B    C
ATOM   1162  N   CYS B  40      29.484  43.231  -3.770  1.00 42.96
B    N
ATOM   1163  CA  CYS B  40      30.174  42.138  -3.125  1.00 42.42
B    C
ATOM   1164  C   CYS B  40      29.968  40.767  -3.775  1.00 42.46
B    C
ATOM   1165  O   CYS B  40      28.844  40.378  -4.077  1.00 42.43
B    O
ATOM   1166  CB  CYS B  40      29.771  42.107  -1.658  1.00 41.23
B    C
ATOM   1167  SG  CYS B  40      30.160  43.644  -0.756  1.00 38.48
B    S
ATOM   1168  N   ARG B  41      31.068  40.041  -3.980  1.00 42.65
B    N
ATOM   1169  CA  ARG B  41      31.038  38.705  -4.584  1.00 43.37
B    C
ATOM   1170  CB  ARG B  41      30.698  38.804  -6.076  1.00 44.07
B    C
ATOM   1171  CG  ARG B  41      30.800  37.482  -6.831  1.00 45.44
B    C
ATOM   1172  CD  ARG B  41      30.385  37.641  -8.290  1.00 46.08
B    C
ATOM   1173  NE  ARG B  41      30.473  36.388  -9.038  1.00 47.65
B    N
ATOM   1174  CZ  ARG B  41      31.612  35.781  -9.356  1.00 47.69
B    C
ATOM   1175  NH1 ARG B  41      32.774  36.307  -8.992  1.00 49.10
B    N
ATOM   1176  NH2 ARG B  41      31.590  34.646 -10.040  1.00 47.59
B    N
ATOM   1177  C   ARG B  41      32.390  38.014  -4.407  1.00 43.67
B    C
ATOM   1178  O   ARG B  41      33.417  38.683  -4.295  1.00 43.52
B    O
ATOM   1179  N   LEU B  42      32.381  36.682  -4.382  1.00 43.47
B    N
ATOM   1180  CA  LEU B  42      33.600  35.902  -4.210  1.00 44.42
B    C
ATOM   1181  CB  LEU B  42      33.695  35.356  -2.774  1.00 42.98
B    C
ATOM   1182  CG  LEU B  42      33.903  36.365  -1.643  1.00 41.64
B    C
ATOM   1183  CD1 LEU B  42      33.743  35.674  -0.299  1.00 41.04
B    C
ATOM   1184  CD2 LEU B  42      35.283  36.981  -1.768  1.00 40.35
B    C
ATOM   1185  C   LEU B  42      33.647  34.744  -5.195  1.00 45.72
B    C
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ATOM   1186  O   LEU B  42      32.635  34.098  -5.470  1.00 45.97
B    O
ATOM   1187  N   ASP B  43      34.834  34.483  -5.735  1.00 46.61
B    N
ATOM   1188  CA  ASP B  43      34.998  33.394  -6.693  1.00 47.21
B    C
ATOM   1189  CB AASP B  43      36.396  33.446  -7.314  0.50 48.39
B    C
ATOM   1190  CB BASP B  43      36.405  33.416  -7.276  0.50 48.20
B    C
ATOM   1191  CG AASP B  43      36.566  32.454  -8.457  0.50 49.57
B    C
ATOM   1192  CG BASP B  43      36.845  34.805  -7.676  0.50 49.13
B    C
ATOM   1193  OD1AASP B  43      35.827  32.564  -9.459  0.50 50.63
B    O
ATOM   1194  OD1BASP B  43      37.622  35.414  -6.914  0.50 50.04
B    O
ATOM   1195  OD2AASP B  43      37.432  31.557  -8.358  0.50 49.95
B    O
ATOM   1196  OD2BASP B  43      36.422  35.282  -8.749  0.50 49.61
B    O
ATOM   1197  C   ASP B  43      34.785  32.037  -6.023  1.00 47.20
B    C
ATOM   1198  O   ASP B  43      35.203  31.836  -4.884  1.00 46.97
B    O
ATOM   1199  N   LYS B  44      34.151  31.108  -6.736  1.00 47.14
B    N
ATOM   1200  CA  LYS B  44      33.869  29.771  -6.212  1.00 46.50
B    C
ATOM   1201  CB  LYS B  44      33.244  28.904  -7.310  1.00 48.36
B    C
ATOM   1202  CG  LYS B  44      31.876  29.408  -7.787  1.00 50.69
B    C
ATOM   1203  CD  LYS B  44      31.231  28.403  -8.735  1.00 52.34
B    C
ATOM   1204  CE  LYS B  44      29.832  28.829  -9.150  1.00 53.13
B    C
ATOM   1205  NZ  LYS B  44      29.175  27.806 -10.015  1.00 54.70
B    N
ATOM   1206  C   LYS B  44      35.121  29.094  -5.665  1.00 45.46
B    C
ATOM   1207  O   LYS B  44      35.083  28.353  -4.677  1.00 45.04
B    O
ATOM   1208  N   SER B  45      36.246  29.362  -6.314  1.00 44.73
B    N
ATOM   1209  CA  SER B  45      37.514  28.777  -5.899  1.00 44.17
B    C
ATOM   1210  CB ASER B  45      38.659  29.317  -6.765  0.50 44.61
B    C
ATOM   1211  CB BSER B  45      38.645  29.351  -6.767  0.50 44.45
B    C
ATOM   1212  OG ASER B  45      39.915  28.799  -6.349  0.50 45.01
B    O
ATOM   1213  OG BSER B  45      38.341  29.256  -8.145  0.50 44.34
B    O
ATOM   1214  C   SER B  45      37.828  29.037  -4.430  1.00 43.68
B    C
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ATOM	1215	O	SER	B	45	38.358	28.164	-3.739	1.00	43.94	B	O
ATOM	1216	N	ASN	B	46	37.504	30.237	-3.958	1.00	43.08	B	N
ATOM	1217	CA	ASN	B	46	37.758	30.613	-2.573	1.00	41.72	B	C
ATOM	1218	CB	ASN	B	46	37.229	32.023	-2.313	1.00	42.60	B	C
ATOM	1219	CG	ASN	B	46	37.938	33.069	-3.134	1.00	42.66	B	C
ATOM	1220	OD1	ASN	B	46	37.794	33.119	-4.353	1.00	43.85	B	O
ATOM	1221	ND2	ASN	B	46	38.726	33.906	-2.471	1.00	43.52	B	N
ATOM	1222	C	ASN	B	46	37.118	29.655	-1.569	1.00	40.56	B	C
ATOM	1223	O	ASN	B	46	37.615	29.501	-0.457	1.00	40.87	B	O
ATOM	1224	N	PHE	B	47	36.012	29.020	-1.949	1.00	39.67	B	N
ATOM	1225	CA	PHE	B	47	35.319	28.103	-1.050	1.00	37.86	B	C
ATOM	1226	CB	PHE	B	47	33.832	28.458	-1.007	1.00	37.18	B	C
ATOM	1227	CG	PHE	B	47	33.549	29.753	-0.297	1.00	38.02	B	C
ATOM	1228	CD1	PHE	B	47	33.520	29.807	1.093	1.00	37.75	B	C
ATOM	1229	CD2	PHE	B	47	33.346	30.928	-1.017	1.00	37.55	B	C
ATOM	1230	CE1	PHE	B	47	33.293	31.013	1.755	1.00	37.90	B	C
ATOM	1231	CE2	PHE	B	47	33.120	32.137	-0.364	1.00	37.70	B	C
ATOM	1232	CZ	PHE	B	47	33.094	32.179	1.024	1.00	37.15	B	C
ATOM	1233	C	PHE	B	47	35.505	26.620	-1.365	1.00	38.38	B	C
ATOM	1234	O	PHE	B	47	34.863	25.764	-0.758	1.00	39.24	B	O
ATOM	1235	N	GLN	B	48	36.379	26.309	-2.313	1.00	37.58	B	N
ATOM	1236	CA	GLN	B	48	36.642	24.915	-2.636	1.00	37.04	B	C
ATOM	1237	CB	GLN	B	48	36.928	24.757	-4.129	1.00	38.28	B	C
ATOM	1238	CG	GLN	B	48	35.687	24.947	-4.988	1.00	40.62	B	C
ATOM	1239	CD	GLN	B	48	35.964	24.815	-6.471	1.00	41.52	B	C
ATOM	1240	OE1	GLN	B	48	35.040	24.827	-7.284	1.00	42.61	B	O
ATOM	1241	NE2	GLN	B	48	37.238	24.692	-6.832	1.00	42.47	B	N
ATOM	1242	C	GLN	B	48	37.835	24.476	-1.793	1.00	35.19	B	C
ATOM	1243	O	GLN	B	48	38.900	24.139	-2.307	1.00	35.18	B	O

ATOM	1244	N	GLN	B	49	37.635	24.504	-0.480	1.00	33.48	B	N
ATOM	1245	CA	GLN	B	49	38.661	24.131	0.484	1.00	32.10	B	C
ATOM	1246	CB	GLN	B	49	39.186	25.377	1.211	1.00	34.97	B	C
ATOM	1247	CG	GLN	B	49	40.433	26.012	0.597	1.00	39.74	B	C
ATOM	1248	CD	GLN	B	49	40.157	26.729	-0.707	1.00	42.56	B	C
ATOM	1249	OE1	GLN	B	49	40.844	26.316	-1.768	1.00	44.68	B	O
ATOM	1250	NE2	GLN	B	49	39.341	27.649	-0.760	1.00	44.50	B	N
ATOM	1251	C	GLN	B	49	38.077	23.157	1.503	1.00	29.66	B	C
ATOM	1252	O	GLN	B	49	37.583	23.569	2.556	1.00	28.91	B	O
ATOM	1253	N	PRO	B	50	38.114	21.850	1.199	1.00	26.63	B	N
ATOM	1254	CD	PRO	B	50	38.639	21.200	-0.013	1.00	26.53	B	C
ATOM	1255	CA	PRO	B	50	37.570	20.860	2.134	1.00	24.12	B	C
ATOM	1256	CB	PRO	B	50	37.720	19.541	1.375	1.00	26.35	B	C
ATOM	1257	CG	PRO	B	50	38.902	19.796	0.468	1.00	26.74	B	C
ATOM	1258	C	PRO	B	50	38.287	20.846	3.476	1.00	20.94	B	C
ATOM	1259	O	PRO	B	50	37.652	20.728	4.522	1.00	20.16	B	O
ATOM	1260	N	TYR	B	51	39.608	20.978	3.451	1.00	18.35	B	N
ATOM	1261	CA	TYR	B	51	40.384	20.964	4.688	1.00	17.88	B	C
ATOM	1262	CB	TYR	B	51	41.877	21.137	4.394	1.00	19.37	B	C
ATOM	1263	CG	TYR	B	51	42.737	21.177	5.638	1.00	18.71	B	C
ATOM	1264	CD1	TYR	B	51	43.015	20.014	6.352	1.00	19.74	B	C
ATOM	1265	CE1	TYR	B	51	43.777	20.043	7.512	1.00	20.59	B	C
ATOM	1266	CD2	TYR	B	51	43.250	22.385	6.118	1.00	20.02	B	C
ATOM	1267	CE2	TYR	B	51	44.018	22.428	7.282	1.00	21.12	B	C
ATOM	1268	CZ	TYR	B	51	44.274	21.253	7.973	1.00	22.10	B	C
ATOM	1269	OH	TYR	B	51	45.008	21.287	9.137	1.00	24.61	B	O
ATOM	1270	C	TYR	B	51	39.933	22.065	5.637	1.00	17.24	B	C
ATOM	1271	O	TYR	B	51	39.560	21.793	6.773	1.00	17.29	B	O
ATOM	1272	N	ILE	B	52	39.969	23.304	5.160	1.00	17.58	B	N

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ATOM   1273  CA  ILE B  52      39.571  24.448   5.973  1.00 21.11
B    C
ATOM   1274  CB  ILE B  52      39.827  25.760   5.210  1.00 24.48
B    C
ATOM   1275  CG2 ILE B  52      39.180  26.934   5.937  1.00 26.45
B    C
ATOM   1276  CG1 ILE B  52      41.342  25.956   5.062  1.00 26.38
B    C
ATOM   1277  CD  ILE B  52      41.748  27.215   4.340  1.00 31.77
B    C
ATOM   1278  C   ILE B  52      38.114  24.378   6.426  1.00 19.79
B    C
ATOM   1279  O   ILE B  52      37.782  24.812   7.530  1.00 20.54
B    O
ATOM   1280  N   THR B  53      37.246  23.834   5.579  1.00 18.58
B    N
ATOM   1281  CA  THR B  53      35.837  23.701   5.932  1.00 17.34
B    C
ATOM   1282  CB  THR B  53      35.032  23.103   4.765  1.00 19.54
B    C
ATOM   1283  OG1 THR B  53      35.186  23.939   3.610  1.00 21.25
B    O
ATOM   1284  CG2 THR B  53      33.558  23.017   5.121  1.00 18.98
B    C
ATOM   1285  C   THR B  53      35.732  22.782   7.146  1.00 16.46
B    C
ATOM   1286  O   THR B  53      35.092  23.116   8.139  1.00 17.44
B    O
ATOM   1287  N   ASN B  54      36.393  21.632   7.074  1.00 16.45
B    N
ATOM   1288  CA  ASN B  54      36.376  20.675   8.178  1.00 15.65
B    C
ATOM   1289  CB  ASN B  54      37.164  19.413   7.806  1.00 17.11
B    C
ATOM   1290  CG  ASN B  54      36.359  18.455   6.942  1.00 19.54
B    C
ATOM   1291  OD1 ASN B  54      35.337  18.827   6.372  1.00 19.10
B    O
ATOM   1292  ND2 ASN B  54      36.826  17.221   6.835  1.00 20.54
B    N
ATOM   1293  C   ASN B  54      36.969  21.288   9.441  1.00 16.14
B    C
ATOM   1294  O   ASN B  54      36.422  21.134  10.535  1.00 16.51
B    O
ATOM   1295  N   ARG B  55      38.087  21.990   9.284  1.00 16.11
B    N
ATOM   1296  CA  ARG B  55      38.748  22.618  10.425  1.00 16.50
B    C
ATOM   1297  CB AARG B  55      40.100  23.214  10.006  0.50 18.63
B    C
ATOM   1298  CB BARG B  55      40.069  23.223  10.002  0.50 18.75
B    C
ATOM   1299  CG AARG B  55      41.043  22.199   9.379  0.50 22.49
B    C
ATOM   1300  CG BARG B  55      41.066  22.263   9.348  0.50 22.67
B    C
ATOM   1301  CD AARG B  55      41.300  21.017  10.307  0.50 25.57
B    C
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ATOM   1302  CD BARG B  55      41.866  21.447  10.363  0.50 26.03
B    C
ATOM   1303  NE AARG B  55      42.403  21.236  11.238  0.50 28.75
B    N
ATOM   1304  NE BARG B  55      41.176  20.260  10.872  0.50 28.52
B    N
ATOM   1305  CZ AARG B  55      42.799  20.343  12.141  0.50 30.20
B    C
ATOM   1306  CZ BARG B  55      41.716  19.416  11.751  0.50 30.40
B    C
ATOM   1307  NH1AARG B  55      42.180  19.173  12.241  0.50 32.50
B    N
ATOM   1308  NH1BARG B  55      42.935  19.643  12.215  0.50 31.14
B    N
ATOM   1309  NH2AARG B  55      43.825  20.611  12.935  0.50 31.35
B    N
ATOM   1310  NH2BARG B  55      41.066  18.325  12.142  0.50 30.17
B    N
ATOM   1311  C   ARG B  55      37.883  23.712  11.041  1.00 13.93
B    C
ATOM   1312  O   ARG B  55      37.924  23.939  12.252  1.00 13.25
B    O
ATOM   1313  N   THR B  56      37.100  24.392  10.208  1.00 14.26
B    N
ATOM   1314  CA  THR B  56      36.230  25.452  10.693  1.00 11.34
B    C
ATOM   1315  CB  THR B  56      35.585  26.237   9.525  1.00 14.38
B    C
ATOM   1316  OG1 THR B  56      36.614  26.908   8.779  1.00 14.44
B    O
ATOM   1317  CG2 THR B  56      34.587  27.266  10.052  1.00 11.15
B    C
ATOM   1318  C   THR B  56      35.149  24.817  11.556  1.00 13.75
B    C
ATOM   1319  O   THR B  56      34.817  25.319  12.631  1.00 14.25
B    O
ATOM   1320  N   PHE B  57      34.598  23.700  11.089  1.00 13.72
B    N
ATOM   1321  CA  PHE B  57      33.565  23.018  11.851  1.00 13.15
B    C
ATOM   1322  CB  PHE B  57      32.899  21.932  11.001  1.00 13.02
B    C
ATOM   1323  CG  PHE B  57      31.799  22.453  10.117  1.00 11.26
B    C
ATOM   1324  CD1 PHE B  57      32.085  23.289   9.044  1.00 12.61
B    C
ATOM   1325  CD2 PHE B  57      30.472  22.125  10.377  1.00 11.56
B    C
ATOM   1326  CE1 PHE B  57      31.069  23.792   8.241  1.00 14.35
B    C
ATOM   1327  CE2 PHE B  57      29.443  22.621   9.582  1.00 11.35
B    C
ATOM   1328  CZ  PHE B  57      29.741  23.458   8.509  1.00 11.81
B    C
ATOM   1329  C   PHE B  57      34.138  22.431  13.142  1.00 13.86
B    C
ATOM   1330  O   PHE B  57      33.444  22.354  14.153  1.00 14.13
B    O
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ATOM   1331  N   MET B  58      35.405  22.029  13.124  1.00 15.45
B    N
ATOM   1332  CA  MET B  58      36.004  21.481  14.335  1.00 16.62
B    C
ATOM   1333  CB  MET B  58      37.325  20.792  14.017  1.00 21.38
B    C
ATOM   1334  CG  MET B  58      37.130  19.435  13.368  1.00 27.49
B    C
ATOM   1335  SD  MET B  58      36.220  18.220  14.333  1.00 33.41
B    S
ATOM   1336  CE  MET B  58      37.378  17.916  15.662  1.00 29.95
B    C
ATOM   1337  C   MET B  58      36.221  22.601  15.343  1.00 15.87
B    C
ATOM   1338  O   MET B  58      36.000  22.429  16.538  1.00 14.52
B    O
ATOM   1339  N   LEU B  59      36.652  23.755  14.852  1.00 14.79
B    N
ATOM   1340  CA  LEU B  59      36.871  24.898  15.719  1.00 13.60
B    C
ATOM   1341  CB  LEU B  59      37.416  26.076  14.910  1.00 12.59
B    C
ATOM   1342  CG  LEU B  59      37.506  27.417  15.643  1.00 12.48
B    C
ATOM   1343  CD1 LEU B  59      38.352  27.260  16.896  1.00 13.58
B    C
ATOM   1344  CD2 LEU B  59      38.105  28.476  14.710  1.00 11.97
B    C
ATOM   1345  C   LEU B  59      35.540  25.283  16.364  1.00 13.10
B    C
ATOM   1346  O   LEU B  59      35.480  25.538  17.566  1.00 14.28
B    O
ATOM   1347  N   ALA B  60      34.477  25.325  15.558  1.00 11.11
B    N
ATOM   1348  CA  ALA B  60      33.145  25.670  16.055  1.00 12.18
B    C
ATOM   1349  CB  ALA B  60      32.148  25.744  14.879  1.00 11.09
B    C
ATOM   1350  C   ALA B  60      32.665  24.659  17.103  1.00 12.00
B    C
ATOM   1351  O   ALA B  60      32.070  25.031  18.119  1.00  9.58
B    O
ATOM   1352  N   LYS B  61      32.915  23.376  16.863  1.00 12.27
B    N
ATOM   1353  CA  LYS B  61      32.515  22.351  17.818  1.00 13.95
B    C
ATOM   1354  CB  LYS B  61      32.842  20.952  17.294  1.00 14.14
B    C
ATOM   1355  CG  LYS B  61      31.862  20.412  16.282  1.00 19.93
B    C
ATOM   1356  CD  LYS B  61      32.281  19.014  15.841  1.00 19.80
B    C
ATOM   1357  CE  LYS B  61      31.339  18.454  14.799  1.00 23.77
B    C
ATOM   1358  NZ  LYS B  61      32.028  17.403  14.007  1.00 22.83
B    N
ATOM   1359  C   LYS B  61      33.228  22.534  19.143  1.00 13.07
B    C
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ATOM   1360  O   LYS B  61      32.611  22.446  20.203  1.00 13.89
B    O
ATOM   1361  N   GLU B  62      34.532  22.782  19.079  1.00 12.95
B    N
ATOM   1362  CA  GLU B  62      35.335  22.955  20.289  1.00 13.90
B    C
ATOM   1363  CB  GLU B  62      36.804  23.164  19.906  1.00 15.80
B    C
ATOM   1364  CG  GLU B  62      37.756  23.426  21.071  1.00 19.60
B    C
ATOM   1365  CD  GLU B  62      37.749  22.321  22.122  1.00 23.26
B    C
ATOM   1366  OE1 GLU B  62      37.759  21.127  21.747  1.00 23.30
B    O
ATOM   1367  OE2 GLU B  62      37.746  22.654  23.332  1.00 25.11
B    O
ATOM   1368  C   GLU B  62      34.841  24.116  21.137  1.00 13.12
B    C
ATOM   1369  O   GLU B  62      34.654  23.974  22.346  1.00 15.86
B    O
ATOM   1370  N   ALA B  63      34.638  25.269  20.509  1.00 12.37
B    N
ATOM   1371  CA  ALA B  63      34.164  26.444  21.228  1.00 11.98
B    C
ATOM   1372  CB  ALA B  63      34.214  27.674  20.322  1.00 10.58
B    C
ATOM   1373  C   ALA B  63      32.743  26.220  21.732  1.00 12.40
B    C
ATOM   1374  O   ALA B  63      32.383  26.695  22.802  1.00 14.78
B    O
ATOM   1375  N   SER B  64      31.938  25.487  20.967  1.00 13.59
B    N
ATOM   1376  CA  SER B  64      30.557  25.225  21.361  1.00 14.14
B    C
ATOM   1377  CB  SER B  64      29.825  24.450  20.266  1.00 13.79
B    C
ATOM   1378  OG  SER B  64      29.537  25.295  19.166  1.00 15.71
B    O
ATOM   1379  C   SER B  64      30.464  24.468  22.680  1.00 16.02
B    C
ATOM   1380  O   SER B  64      29.456  24.576  23.389  1.00 14.81
B    O
ATOM   1381  N   LEU B  65      31.516  23.715  23.009  1.00 16.10
B    N
ATOM   1382  CA  LEU B  65      31.546  22.951  24.258  1.00 18.41
B    C
ATOM   1383  CB  LEU B  65      32.829  22.124  24.362  1.00 19.27
B    C
ATOM   1384  CG  LEU B  65      33.084  21.082  23.277  1.00 19.94
B    C
ATOM   1385  CD1 LEU B  65      34.420  20.401  23.556  1.00 21.12
B    C
ATOM   1386  CD2 LEU B  65      31.941  20.069  23.233  1.00 19.85
B    C
ATOM   1387  C   LEU B  65      31.461  23.873  25.472  1.00 21.28
B    C
ATOM   1388  O   LEU B  65      30.913  23.496  26.508  1.00 20.85
B    O
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ATOM   1389  N   ALA B  66      31.993  25.084  25.337  1.00 22.77
B    N
ATOM   1390  CA  ALA B  66      31.991  26.041  26.440  1.00 23.05
B    C
ATOM   1391  CB  ALA B  66      33.340  26.759  26.505  1.00 23.03
B    C
ATOM   1392  C   ALA B  66      30.864  27.063  26.349  1.00 25.33
B    C
ATOM   1393  O   ALA B  66      30.794  27.989  27.160  1.00 24.62
B    O
ATOM   1394  N   ASP B  67      29.984  26.895  25.366  1.00 24.71
B    N
ATOM   1395  CA  ASP B  67      28.859  27.805  25.169  1.00 24.59
B    C
ATOM   1396  CB  ASP B  67      28.843  28.293  23.715  1.00 21.80
B    C
ATOM   1397  CG  ASP B  67      27.658  29.193  23.409  1.00 23.11
B    C
ATOM   1398  OD1 ASP B  67      27.492  30.220  24.101  1.00 21.79
B    O
ATOM   1399  OD2 ASP B  67      26.894  28.881  22.468  1.00 22.86
B    O
ATOM   1400  C   ASP B  67      27.539  27.105  25.484  1.00 24.11
B    C
ATOM   1401  O   ASP B  67      27.339  25.961  25.090  1.00 24.85
B    O
ATOM   1402  N   ASN B  68      26.643  27.781  26.199  1.00 23.66
B    N
ATOM   1403  CA  ASN B  68      25.341  27.190  26.505  1.00 26.10
B    C
ATOM   1404  CB  ASN B  68      24.606  27.991  27.584  1.00 26.12
B    C
ATOM   1405  CG  ASN B  68      23.178  27.507  27.791  1.00 28.10
B    C
ATOM   1406  OD1 ASN B  68      22.902  26.309  27.704  1.00 30.31
B    O
ATOM   1407  ND2 ASN B  68      22.267  28.432  28.075  1.00 29.58
B    N
ATOM   1408  C   ASN B  68      24.514  27.191  25.223  1.00 26.09
B    C
ATOM   1409  O   ASN B  68      24.122  28.252  24.733  1.00 25.01
B    O
ATOM   1410  N   ASN B  69      24.245  26.006  24.682  1.00 26.55
B    N
ATOM   1411  CA  ASN B  69      23.488  25.905  23.435  1.00 28.23
B    C
ATOM   1412  CB  ASN B  69      23.321  24.443  23.029  1.00 29.69
B    C
ATOM   1413  CG  ASN B  69      24.642  23.743  22.885  1.00 32.95
B    C
ATOM   1414  OD1 ASN B  69      25.616  24.339  22.428  1.00 33.35
B    O
ATOM   1415  ND2 ASN B  69      24.690  22.470  23.268  1.00 35.41
B    N
ATOM   1416  C   ASN B  69      22.129  26.575  23.462  1.00 27.38
B    C
ATOM   1417  O   ASN B  69      21.754  27.280  22.527  1.00 26.91
B    O
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ATOM   1418  N   THR B  70      21.386  26.367  24.533  1.00 27.43
B    N
ATOM   1419  CA  THR B  70      20.063  26.963  24.620  1.00 31.14
B    C
ATOM   1420  CB  THR B  70      19.290  26.312  25.724  1.00 33.84
B    C
ATOM   1421  OG1 THR B  70      20.017  26.483  26.949  1.00 38.79
B    O
ATOM   1422  CG2 THR B  70      19.099  24.825  25.414  1.00 35.38
B    C
ATOM   1423  C   THR B  70      20.084  28.472  24.850  1.00 29.99
B    C
ATOM   1424  O   THR B  70      19.032  29.100  24.983  1.00 31.80
B    O
ATOM   1425  N   ASP B  71      21.280  29.048  24.900  1.00 28.37
B    N
ATOM   1426  CA  ASP B  71      21.420  30.481  25.102  1.00 25.20
B    C
ATOM   1427  CB  ASP B  71      22.838  30.798  25.589  1.00 24.99
B    C
ATOM   1428  CG  ASP B  71      22.995  32.241  26.019  1.00 25.37
B    C
ATOM   1429  OD1 ASP B  71      21.991  32.842  26.457  1.00 24.56
B    O
ATOM   1430  OD2 ASP B  71      24.120  32.775  25.929  1.00 24.43
B    O
ATOM   1431  C   ASP B  71      21.124  31.210  23.789  1.00 24.70
B    C
ATOM   1432  O   ASP B  71      20.958  30.579  22.741  1.00 25.80
B    O
ATOM   1433  N   VAL B  72      21.051  32.536  23.852  1.00 22.24
B    N
ATOM   1434  CA  VAL B  72      20.769  33.352  22.674  1.00 21.58
B    C
ATOM   1435  CB  VAL B  72      20.887  34.856  23.015  1.00 21.53
B    C
ATOM   1436  CG1 VAL B  72      22.310  35.177  23.443  1.00 21.59
B    C
ATOM   1437  CG2 VAL B  72      20.468  35.711  21.818  1.00 24.37
B    C
ATOM   1438  C   VAL B  72      21.729  33.005  21.534  1.00 21.11
B    C
ATOM   1439  O   VAL B  72      22.864  32.600  21.773  1.00 17.71
B    O
ATOM   1440  N   ARG B  73      21.259  33.162  20.300  1.00 19.03
B    N
ATOM   1441  CA  ARG B  73      22.062  32.861  19.120  1.00 21.00
B    C
ATOM   1442  CB  ARG B  73      21.242  32.005  18.145  1.00 20.05
B    C
ATOM   1443  CG  ARG B  73      20.914  30.607  18.658  1.00 22.93
B    C
ATOM   1444  CD  ARG B  73      22.184  29.788  18.848  1.00 23.32
B    C
ATOM   1445  NE  ARG B  73      22.541  29.607  20.253  1.00 26.02
B    N
ATOM   1446  CZ  ARG B  73      23.792  29.534  20.701  1.00 28.62
B    C
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ATOM   1447  NH1 ARG B  73      24.810  29.643  19.850  1.00 27.83
B    N
ATOM   1448  NH2 ARG B  73      24.032  29.318  21.991  1.00 24.28
B    N
ATOM   1449  C   ARG B  73      22.562  34.130  18.422  1.00 19.92
B    C
ATOM   1450  O   ARG B  73      22.231  35.242  18.823  1.00 23.35
B    O
ATOM   1451  N   LEU B  74      23.361  33.956  17.375  1.00 18.84
B    N
ATOM   1452  CA  LEU B  74      23.928  35.091  16.644  1.00 18.10
B    C
ATOM   1453  CB  LEU B  74      25.452  35.071  16.764  1.00 17.88
B    C
ATOM   1454  CG  LEU B  74      26.021  35.213  18.178  1.00 17.88
B    C
ATOM   1455  CD1 LEU B  74      27.514  34.966  18.146  1.00 19.62
B    C
ATOM   1456  CD2 LEU B  74      25.711  36.602  18.727  1.00 16.68
B    C
ATOM   1457  C   LEU B  74      23.550  35.113  15.172  1.00 18.69
B    C
ATOM   1458  O   LEU B  74      22.990  36.094  14.678  1.00 17.25
B    O
ATOM   1459  N   ILE B  75      23.864  34.026  14.478  1.00 18.86
B    N
ATOM   1460  CA  ILE B  75      23.565  33.900  13.055  1.00 19.94
B    C
ATOM   1461  CB AILE B  75      24.683  33.133  12.315  0.50 19.70
B    C
ATOM   1462  CB BILE B  75      24.685  33.159  12.306  0.50 19.21
B    C
ATOM   1463  CG2AILE B  75      24.354  33.044  10.830  0.50 20.21
B    C
ATOM   1464  CG2BILE B  75      24.280  32.922  10.857  0.50 19.75
B    C
ATOM   1465  CG1AILE B  75      26.032  33.829  12.533  0.50 21.96
B    C
ATOM   1466  CG1BILE B  75      25.976  33.983  12.354  0.50 20.78
B    C
ATOM   1467  CD AILE B  75      26.075  35.259  12.036  0.50 21.49
B    C
ATOM   1468  CD BILE B  75      27.167  33.330  11.684  0.50 19.44
B    C
ATOM   1469  C   ILE B  75      22.250  33.159  12.850  1.00 19.75
B    C
ATOM   1470  O   ILE B  75      22.118  32.001  13.241  1.00 19.53
B    O
ATOM   1471  N   GLY B  76      21.279  33.834  12.244  1.00 20.72
B    N
ATOM   1472  CA  GLY B  76      19.991  33.215  12.002  1.00 21.85
B    C
ATOM   1473  C   GLY B  76      19.144  34.080  11.090  1.00 23.94
B    C
ATOM   1474  O   GLY B  76      19.583  35.137  10.625  1.00 21.15
B    O
ATOM   1475  N   GLU B  77      17.915  33.637  10.849  1.00 24.76
B    N
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ATOM   1476  CA  GLU B  77      16.994  34.355   9.981  1.00 25.59
B    C
ATOM   1477  CB  GLU B  77      15.622  33.683  10.024  1.00 28.23
B    C
ATOM   1478  CG  GLU B  77      14.939  33.702  11.385  1.00 29.97
B    C
ATOM   1479  CD  GLU B  77      14.300  35.043  11.702  1.00 31.49
B    C
ATOM   1480  OE1 GLU B  77      13.646  35.618  10.805  1.00 31.82
B    O
ATOM   1481  OE2 GLU B  77      14.438  35.516  12.851  1.00 32.75
B    O
ATOM   1482  C   GLU B  77      16.863  35.826  10.340  1.00 26.42
B    C
ATOM   1483  O   GLU B  77      16.733  36.667   9.454  1.00 25.64
B    O
ATOM   1484  N   LYS B  78      16.903  36.141  11.632  1.00 26.48
B    N
ATOM   1485  CA  LYS B  78      16.769  37.529  12.071  1.00 26.66
B    C
ATOM   1486  CB  LYS B  78      16.769  37.614  13.607  1.00 29.51
B    C
ATOM   1487  CG  LYS B  78      17.949  36.911  14.306  1.00 34.38
B    C
ATOM   1488  CD  LYS B  78      17.866  35.363  14.172  1.00 34.31
B    C
ATOM   1489  CE  LYS B  78      19.033  34.584  14.838  1.00 35.41
B    C
ATOM   1490  NZ  LYS B  78      19.360  35.086  16.206  1.00 33.27
B    N
ATOM   1491  C   LYS B  78      17.845  38.439  11.488  1.00 25.68
B    C
ATOM   1492  O   LYS B  78      17.585  39.607  11.182  1.00 25.09
B    O
ATOM   1493  N   LEU B  79      19.049  37.903  11.322  1.00 22.46
B    N
ATOM   1494  CA  LEU B  79      20.158  38.663  10.759  1.00 22.51
B    C
ATOM   1495  CB  LEU B  79      21.421  37.790  10.744  1.00 21.91
B    C
ATOM   1496  CG  LEU B  79      22.765  38.360  10.272  1.00 21.91
B    C
ATOM   1497  CD1 LEU B  79      23.199  39.526  11.164  1.00 20.83
B    C
ATOM   1498  CD2 LEU B  79      23.819  37.255  10.317  1.00 18.82
B    C
ATOM   1499  C   LEU B  79      19.833  39.125   9.332  1.00 23.76
B    C
ATOM   1500  O   LEU B  79      20.355  40.139   8.858  1.00 21.25
B    O
ATOM   1501  N   PHE B  80      18.957  38.389   8.655  1.00 23.14
B    N
ATOM   1502  CA  PHE B  80      18.605  38.721   7.283  1.00 24.04
B    C
ATOM   1503  CB  PHE B  80      18.576  37.448   6.434  1.00 22.67
B    C
ATOM   1504  CG  PHE B  80      19.852  36.665   6.484  1.00 22.24
B    C
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ATOM   1505  CD1 PHE B  80      20.086  35.754   7.508  1.00 22.35
B    C
ATOM   1506  CD2 PHE B  80      20.837  36.863   5.527  1.00 22.73
B    C
ATOM   1507  CE1 PHE B  80      21.286  35.051   7.578  1.00 23.09
B    C
ATOM   1508  CE2 PHE B  80      22.039  36.164   5.591  1.00 24.92
B    C
ATOM   1509  CZ  PHE B  80      22.262  35.255   6.622  1.00 23.28
B    C
ATOM   1510  C   PHE B  80      17.289  39.474   7.113  1.00 25.53
B    C
ATOM   1511  O   PHE B  80      16.817  39.650   5.989  1.00 25.25
B    O
ATOM   1512  N   HIS B  81      16.705  39.928   8.218  1.00 26.38
B    N
ATOM   1513  CA  HIS B  81      15.444  40.662   8.192  1.00 27.94
B    C
ATOM   1514  CB AHIS B  81      15.100  41.146   9.593  0.50 31.29
B    C
ATOM   1515  CB BHIS B  81      15.009  41.082   9.560  0.50 31.04
B    C
ATOM   1516  CG AHIS B  81      13.748  41.770   9.701  0.50 34.69
B    C
ATOM   1517  CG BHIS B  81      14.361  40.000  10.367  0.50 33.94
B    C
ATOM   1518  CD2AHIS B  81      12.617  41.581   8.966  0.50 35.93
B    C
ATOM   1519  CD2BHIS B  81      14.072  38.713  10.063  0.50 35.25
B    C
ATOM   1520  ND1AHIS B  81      13.422  42.706  10.655  0.50 36.16
B    N
ATOM   1521  ND1BHIS B  81      13.923  40.196  11.660  0.50 35.74
B    N
ATOM   1522  CE1AHIS B  81      12.158  43.070  10.511  0.50 37.27
B    C
ATOM   1523  CE1BHIS B  81      13.393  39.075  12.117  0.50 36.86
B    C
ATOM   1524  NE2AHIS B  81      11.653  42.400   9.493  0.50 37.17
B    N
ATOM   1525  NE2BHIS B  81      13.470  38.160  11.168  0.50 36.06
B    N
ATOM   1526  C   HIS B  81      15.507  41.870   7.260  1.00 27.52
B    C
ATOM   1527  O   HIS B  81      16.309  42.781   7.473  1.00 27.00
B    O
ATOM   1528  N   GLY B  82      14.685  41.857   6.213  1.00 26.26
B    N
ATOM   1529  CA  GLY B  82      14.667  42.960   5.270  1.00 24.51
B    C
ATOM   1530  C   GLY B  82      15.874  43.081   4.366  1.00 24.60
B    C
ATOM   1531  O   GLY B  82      16.060  44.108   3.722  1.00 25.03
B    O
ATOM   1532  N   VAL B  83      16.702  42.044   4.317  1.00 26.22
B    N
ATOM   1533  CA  VAL B  83      17.894  42.058   3.474  1.00 24.22
B    C
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ATOM   1534  CB  VAL B  83      19.099  41.422   4.198  1.00 23.59
B    C
ATOM   1535  CG1 VAL B  83      20.338  41.501   3.315  1.00 21.40
B    C
ATOM   1536  CG2 VAL B  83      19.332  42.121   5.526  1.00 20.96
B    C
ATOM   1537  C   VAL B  83      17.635  41.282   2.188  1.00 26.23
B    C
ATOM   1538  O   VAL B  83      17.400  40.078   2.220  1.00 26.03
B    O
ATOM   1539  N   SER B  84      17.671  41.974   1.055  1.00 29.00
B    N
ATOM   1540  CA  SER B  84      17.438  41.317  -0.226  1.00 31.27
B    C
ATOM   1541  CB  SER B  84      17.307  42.360  -1.341  1.00 31.72
B    C
ATOM   1542  OG  SER B  84      18.503  43.103  -1.500  1.00 34.12
B    O
ATOM   1543  C   SER B  84      18.599  40.374  -0.522  1.00 32.20
B    C
ATOM   1544  O   SER B  84      19.659  40.476   0.099  1.00 31.68
B    O
ATOM   1545  N   MET B  85      18.396  39.454  -1.462  1.00 32.77
B    N
ATOM   1546  CA  MET B  85      19.434  38.492  -1.837  1.00 33.78
B    C
ATOM   1547  CB  MET B  85      18.916  37.542  -2.925  1.00 36.68
B    C
ATOM   1548  CG  MET B  85      17.883  36.545  -2.439  1.00 40.28
B    C
ATOM   1549  SD  MET B  85      18.469  35.551  -1.056  1.00 48.72
B    S
ATOM   1550  CE  MET B  85      19.962  34.852  -1.742  1.00 44.99
B    C
ATOM   1551  C   MET B  85      20.704  39.167  -2.342  1.00 32.27
B    C
ATOM   1552  O   MET B  85      21.814  38.650  -2.165  1.00 33.11
B    O
ATOM   1553  N   SER B  86      20.538  40.323  -2.971  1.00 30.58
B    N
ATOM   1554  CA  SER B  86      21.669  41.053  -3.521  1.00 31.46
B    C
ATOM   1555  CB  SER B  86      21.187  42.065  -4.573  1.00 32.63
B    C
ATOM   1556  OG  SER B  86      20.319  43.052  -4.031  1.00 39.50
B    O
ATOM   1557  C   SER B  86      22.492  41.774  -2.471  1.00 29.04
B    C
ATOM   1558  O   SER B  86      23.608  42.227  -2.746  1.00 28.91
B    O
ATOM   1559  N   GLU B  87      21.941  41.863  -1.265  1.00 26.59
B    N
ATOM   1560  CA  GLU B  87      22.608  42.539  -0.162  1.00 24.76
B    C
ATOM   1561  CB  GLU B  87      21.601  43.420   0.581  1.00 25.49
B    C
ATOM   1562  CG  GLU B  87      20.847  44.392  -0.313  1.00 29.17
B    C
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ATOM   1563  CD  GLU B  87      19.853  45.248   0.449  1.00 30.87
B     C
ATOM   1564  OE1 GLU B  87      19.028  44.689   1.206  1.00 30.33
B     O
ATOM   1565  OE2 GLU B  87      19.891  46.484   0.283  1.00 35.00
B     O
ATOM   1566  C   GLU B  87      23.257  41.563   0.821  1.00 23.73
B     C
ATOM   1567  O   GLU B  87      24.029  41.972   1.685  1.00 21.32
B     O
ATOM   1568  N   ARG B  88      22.957  40.276   0.676  1.00 22.70
B     N
ATOM   1569  CA  ARG B  88      23.499  39.261   1.578  1.00 24.54
B     C
ATOM   1570  CB  ARG B  88      22.967  37.881   1.194  1.00 25.66
B     C
ATOM   1571  CG  ARG B  88      21.509  37.681   1.537  1.00 27.47
B     C
ATOM   1572  CD  ARG B  88      21.118  36.224   1.391  1.00 29.90
B     C
ATOM   1573  NE  ARG B  88      19.755  35.977   1.853  1.00 33.50
B     N
ATOM   1574  CZ  ARG B  88      19.197  34.772   1.926  1.00 34.03
B     C
ATOM   1575  NH1 ARG B  88      19.888  33.699   1.569  1.00 34.95
B     N
ATOM   1576  NH2 ARG B  88      17.947  34.642   2.350  1.00 35.52
B     N
ATOM   1577  C   ARG B  88      25.018  39.187   1.727  1.00 23.31
B     C
ATOM   1578  O   ARG B  88      25.522  39.058   2.841  1.00 23.06
B     O
ATOM   1579  N   CYS B  89      25.756  39.256   0.626  1.00 23.32
B     N
ATOM   1580  CA  CYS B  89      27.208  39.170   0.739  1.00 22.87
B     C
ATOM   1581  C   CYS B  89      27.778  40.378   1.486  1.00 22.34
B     C
ATOM   1582  O   CYS B  89      28.706  40.238   2.287  1.00 20.71
B     O
ATOM   1583  CB  CYS B  89      27.865  39.037  -0.639  1.00 22.30
B     C
ATOM   1584  SG  CYS B  89      29.668  38.836  -0.507  1.00 24.58
B     S
ATOM   1585  N   TYR B  90      27.207  41.555   1.232  1.00 22.12
B     N
ATOM   1586  CA  TYR B  90      27.636  42.786   1.891  1.00 21.33
B     C
ATOM   1587  CB  TYR B  90      26.896  43.990   1.307  1.00 24.19
B     C
ATOM   1588  CG  TYR B  90      27.227  45.299   1.989  1.00 25.69
B     C
ATOM   1589  CD1 TYR B  90      28.484  45.897   1.838  1.00 26.69
B     C
ATOM   1590  CE1 TYR B  90      28.795  47.101   2.483  1.00 26.25
B     C
ATOM   1591  CD2 TYR B  90      26.290  45.933   2.803  1.00 26.17
B     C
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ATOM   1592  CE2 TYR B  90      26.591  47.130   3.452  1.00 27.02
B    C
ATOM   1593  CZ  TYR B  90      27.842  47.707   3.288  1.00 26.75
B    C
ATOM   1594  OH  TYR B  90      28.129  48.891   3.925  1.00 28.36
B    O
ATOM   1595  C   TYR B  90      27.310  42.652   3.375  1.00 20.94
B    C
ATOM   1596  O   TYR B  90      28.081  43.075   4.239  1.00 21.09
B    O
ATOM   1597  N   LEU B  91      26.156  42.065   3.658  1.00 17.63
B    N
ATOM   1598  CA  LEU B  91      25.724  41.828   5.031  1.00 18.40
B    C
ATOM   1599  CB  LEU B  91      24.349  41.158   5.025  1.00 19.21
B    C
ATOM   1600  CG  LEU B  91      23.874  40.595   6.361  1.00 22.33
B    C
ATOM   1601  CD1 LEU B  91      23.538  41.736   7.296  1.00 19.22
B    C
ATOM   1602  CD2 LEU B  91      22.657  39.700   6.137  1.00 23.86
B    C
ATOM   1603  C   LEU B  91      26.734  40.912   5.741  1.00 17.20
B    C
ATOM   1604  O   LEU B  91      27.210  41.211   6.841  1.00 17.10
B    O
ATOM   1605  N   MET B  92      27.056  39.791   5.107  1.00 16.43
B    N
ATOM   1606  CA  MET B  92      27.997  38.847   5.685  1.00 17.07
B    C
ATOM   1607  CB  MET B  92      28.002  37.552   4.871  1.00 16.48
B    C
ATOM   1608  CG  MET B  92      26.703  36.752   4.979  1.00 17.63
B    C
ATOM   1609  SD  MET B  92      26.128  36.605   6.690  1.00 17.99
B    S
ATOM   1610  CE  MET B  92      27.492  35.700   7.425  1.00 14.17
B    C
ATOM   1611  C   MET B  92      29.410  39.430   5.790  1.00 18.87
B    C
ATOM   1612  O   MET B  92      30.187  39.048   6.670  1.00 17.61
B    O
ATOM   1613  N   LYS B  93      29.747  40.350   4.891  1.00 20.69
B    N
ATOM   1614  CA  LYS B  93      31.060  40.988   4.936  1.00 20.45
B    C
ATOM   1615  CB  LYS B  93      31.219  41.984   3.791  1.00 21.79
B    C
ATOM   1616  CG  LYS B  93      32.527  42.755   3.838  1.00 22.89
B    C
ATOM   1617  CD  LYS B  93      32.490  43.949   2.892  1.00 27.03
B    C
ATOM   1618  CE  LYS B  93      33.765  44.778   2.995  1.00 28.50
B    C
ATOM   1619  NZ  LYS B  93      33.700  46.001   2.138  1.00 30.45
B    N
ATOM   1620  C   LYS B  93      31.181  41.732   6.267  1.00 19.66
B    C
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ATOM   1621  O   LYS B  93      32.200  41.649   6.946  1.00 19.17
B    O
ATOM   1622  N   GLN B  94      30.131  42.456   6.637  1.00 19.14
B    N
ATOM   1623  CA  GLN B  94      30.136  43.201   7.890  1.00 19.70
B    C
ATOM   1624  CB  GLN B  94      28.814  43.956   8.061  1.00 21.16
B    C
ATOM   1625  CG  GLN B  94      28.392  44.765   6.844  1.00 22.73
B    C
ATOM   1626  CD  GLN B  94      29.451  45.752   6.397  1.00 22.05
B    C
ATOM   1627  OE1 GLN B  94      29.802  45.806   5.217  1.00 26.54
B    O
ATOM   1628  NE2 GLN B  94      29.963  46.541   7.333  1.00 18.51
B    N
ATOM   1629  C   GLN B  94      30.329  42.244   9.071  1.00 18.12
B    C
ATOM   1630  O   GLN B  94      31.121  42.510   9.980  1.00 17.93
B    O
ATOM   1631  N   VAL B  95      29.592  41.138   9.055  1.00 14.83
B    N
ATOM   1632  CA  VAL B  95      29.679  40.140  10.117  1.00 13.76
B    C
ATOM   1633  CB  VAL B  95      28.635  39.025   9.906  1.00 13.80
B    C
ATOM   1634  CG1 VAL B  95      28.812  37.932  10.944  1.00 12.84
B    C
ATOM   1635  CG2 VAL B  95      27.246  39.611   9.997  1.00 11.25
B    C
ATOM   1636  C   VAL B  95      31.079  39.529  10.149  1.00 13.82
B    C
ATOM   1637  O   VAL B  95      31.690  39.410  11.211  1.00 13.76
B    O
ATOM   1638  N   LEU B  96      31.583  39.149   8.980  1.00 14.12
B    N
ATOM   1639  CA  LEU B  96      32.918  38.570   8.870  1.00 15.35
B    C
ATOM   1640  CB  LEU B  96      33.251  38.298   7.403  1.00 15.65
B    C
ATOM   1641  CG  LEU B  96      34.721  37.969   7.126  1.00 16.49
B    C
ATOM   1642  CD1 LEU B  96      35.100  36.677   7.833  1.00 13.79
B    C
ATOM   1643  CD2 LEU B  96      34.947  37.856   5.628  1.00 15.98
B    C
ATOM   1644  C   LEU B  96      34.010  39.471   9.465  1.00 16.84
B    C
ATOM   1645  O   LEU B  96      34.856  39.007  10.238  1.00 16.28
B    O
ATOM   1646  N   ASN B  97      33.994  40.752   9.097  1.00 15.44
B    N
ATOM   1647  CA  ASN B  97      34.997  41.699   9.590  1.00 16.09
B    C
ATOM   1648  CB  ASN B  97      34.901  43.021   8.821  1.00 17.20
B    C
ATOM   1649  CG  ASN B  97      35.362  42.873   7.385  1.00 18.71
B    C
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ATOM   1650  OD1 ASN B  97      36.125  41.961   7.081  1.00 18.61
B    O
ATOM   1651  ND2 ASN B  97      34.910  43.761   6.499  1.00 17.57
B    N
ATOM   1652  C   ASN B  97      34.896  41.940  11.085  1.00 15.40
B    C
ATOM   1653  O   ASN B  97      35.914  42.005  11.777  1.00 16.22
B    O
ATOM   1654  N   PHE B  98      33.673  42.066  11.588  1.00 14.94
B    N
ATOM   1655  CA  PHE B  98      33.476  42.266  13.017  1.00 14.55
B    C
ATOM   1656  CB  PHE B  98      31.986  42.369  13.356  1.00 13.40
B    C
ATOM   1657  CG  PHE B  98      31.700  42.315  14.834  1.00 15.06
B    C
ATOM   1658  CD1 PHE B  98      31.958  43.415  15.649  1.00 14.98
B    C
ATOM   1659  CD2 PHE B  98      31.200  41.150  15.418  1.00 14.58
B    C
ATOM   1660  CE1 PHE B  98      31.720  43.360  17.032  1.00 14.56
B    C
ATOM   1661  CE2 PHE B  98      30.957  41.077  16.799  1.00 13.20
B    C
ATOM   1662  CZ  PHE B  98      31.218  42.188  17.608  1.00 12.63
B    C
ATOM   1663  C   PHE B  98      34.055  41.074  13.764  1.00 14.69
B    C
ATOM   1664  O   PHE B  98      34.793  41.227  14.735  1.00 14.16
B    O
ATOM   1665  N   THR B  99      33.705  39.880  13.300  1.00 14.39
B    N
ATOM   1666  CA  THR B  99      34.154  38.651  13.932  1.00 13.57
B    C
ATOM   1667  CB  THR B  99      33.490  37.433  13.257  1.00 12.94
B    C
ATOM   1668  OG1 THR B  99      32.059  37.576  13.316  1.00 12.53
B    O
ATOM   1669  CG2 THR B  99      33.896  36.143  13.958  1.00 12.70
B    C
ATOM   1670  C   THR B  99      35.677  38.516  13.893  1.00 13.81
B    C
ATOM   1671  O   THR B  99      36.295  38.142  14.884  1.00 12.81
B    O
ATOM   1672  N   LEU B 100      36.285  38.830  12.754  1.00 14.39
B    N
ATOM   1673  CA  LEU B 100      37.735  38.732  12.645  1.00 15.17
B    C
ATOM   1674  CB  LEU B 100      38.181  39.035  11.213  1.00 17.01
B    C
ATOM   1675  CG  LEU B 100      38.047  37.902  10.187  1.00 19.42
B    C
ATOM   1676  CD1 LEU B 100      38.195  38.470   8.778  1.00 20.62
B    C
ATOM   1677  CD2 LEU B 100      39.105  36.830  10.460  1.00 19.19
B    C
ATOM   1678  C   LEU B 100      38.439  39.694  13.608  1.00 16.32
B    C
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ATOM   1679  O   LEU B 100      39.276  39.289  14.412  1.00 15.91
B    O
ATOM   1680  N   GLU B 101      38.079  40.968  13.533  1.00 15.77
B    N
ATOM   1681  CA  GLU B 101      38.717  41.982  14.365  1.00 17.05
B    C
ATOM   1682  CB  GLU B 101      38.439  43.370  13.781  1.00 20.26
B    C
ATOM   1683  CG  GLU B 101      39.123  43.627  12.449  1.00 25.68
B    C
ATOM   1684  CD  GLU B 101      38.898  45.038  11.941  1.00 29.94
B    C
ATOM   1685  OE1 GLU B 101      39.087  45.992  12.730  1.00 31.04
B    O
ATOM   1686  OE2 GLU B 101      38.541  45.192  10.752  1.00 31.88
B    O
ATOM   1687  C   GLU B 101      38.366  41.992  15.846  1.00 15.48
B    C
ATOM   1688  O   GLU B 101      39.232  42.214  16.684  1.00 14.15
B    O
ATOM   1689  N   GLU B 102      37.103  41.749  16.169  1.00 14.59
B    N
ATOM   1690  CA  GLU B 102      36.664  41.792  17.558  1.00 16.25
B    C
ATOM   1691  CB  GLU B 102      35.292  42.462  17.624  1.00 15.08
B    C
ATOM   1692  CG  GLU B 102      35.257  43.884  17.055  1.00 16.02
B    C
ATOM   1693  CD  GLU B 102      35.992  44.893  17.928  1.00 15.88
B    C
ATOM   1694  OE1 GLU B 102      35.953  44.745  19.168  1.00 15.08
B    O
ATOM   1695  OE2 GLU B 102      36.595  45.846  17.383  1.00 15.59
B    O
ATOM   1696  C   GLU B 102      36.611  40.451  18.283  1.00 17.63
B    C
ATOM   1697  O   GLU B 102      36.475  40.408  19.510  1.00 16.52
B    O
ATOM   1698  N   VAL B 103      36.721  39.357  17.539  1.00 16.71
B    N
ATOM   1699  CA  VAL B 103      36.660  38.039  18.151  1.00 16.91
B    C
ATOM   1700  CB  VAL B 103      35.392  37.286  17.709  1.00 16.05
B    C
ATOM   1701  CG1 VAL B 103      35.394  35.881  18.310  1.00 19.19
B    C
ATOM   1702  CG2 VAL B 103      34.157  38.054  18.144  1.00 18.67
B    C
ATOM   1703  C   VAL B 103      37.845  37.128  17.862  1.00 17.70
B    C
ATOM   1704  O   VAL B 103      38.540  36.680  18.784  1.00 16.69
B    O
ATOM   1705  N   LEU B 104      38.067  36.855  16.581  1.00 16.37
B    N
ATOM   1706  CA  LEU B 104      39.137  35.960  16.168  1.00 18.90
B    C
ATOM   1707  CB  LEU B 104      38.984  35.614  14.687  1.00 15.60
B    C
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ATOM   1708  CG  LEU B 104      37.636  34.955  14.362  1.00 16.30
B    C
ATOM   1709  CD1 LEU B 104      37.541  34.663  12.874  1.00 14.16
B    C
ATOM   1710  CD2 LEU B 104      37.485  33.671  15.162  1.00 16.44
B    C
ATOM   1711  C   LEU B 104      40.539  36.471  16.447  1.00 20.44
B    C
ATOM   1712  O   LEU B 104      41.326  35.780  17.086  1.00 20.16
B    O
ATOM   1713  N   PHE B 105      40.870  37.666  15.979  1.00 21.99
B    N
ATOM   1714  CA  PHE B 105      42.213  38.166  16.239  1.00 27.13
B    C
ATOM   1715  CB  PHE B 105      42.387  39.579  15.675  1.00 28.81
B    C
ATOM   1716  CG  PHE B 105      42.367  39.634  14.168  1.00 31.64
B    C
ATOM   1717  CD1 PHE B 105      42.837  38.563  13.411  1.00 33.85
B    C
ATOM   1718  CD2 PHE B 105      41.888  40.757  13.506  1.00 34.49
B    C
ATOM   1719  CE1 PHE B 105      42.831  38.611  12.015  1.00 34.86
B    C
ATOM   1720  CE2 PHE B 105      41.879  40.816  12.110  1.00 35.62
B    C
ATOM   1721  CZ  PHE B 105      42.351  39.739  11.365  1.00 35.69
B    C
ATOM   1722  C   PHE B 105      42.538  38.122  17.734  1.00 27.95
B    C
ATOM   1723  O   PHE B 105      43.607  37.656  18.121  1.00 28.77
B    O
ATOM   1724  N   PRO B 106      41.613  38.587  18.594  1.00 28.70
B    N
ATOM   1725  CD  PRO B 106      40.390  39.341  18.266  1.00 28.83
B    C
ATOM   1726  CA  PRO B 106      41.836  38.578  20.045  1.00 27.96
B    C
ATOM   1727  CB  PRO B 106      40.590  39.280  20.589  1.00 28.83
B    C
ATOM   1728  CG  PRO B 106      40.223  40.214  19.481  1.00 28.82
B    C
ATOM   1729  C   PRO B 106      41.991  37.166  20.622  1.00 27.58
B    C
ATOM   1730  O   PRO B 106      42.607  36.983  21.671  1.00 25.86
B    O
ATOM   1731  N   GLN B 107      41.419  36.174  19.945  1.00 26.57
B    N
ATOM   1732  CA  GLN B 107      41.499  34.784  20.394  1.00 27.34
B    C
ATOM   1733  CB  GLN B 107      40.119  34.123  20.321  1.00 25.90
B    C
ATOM   1734  CG  GLN B 107      39.027  34.737  21.181  1.00 27.05
B    C
ATOM   1735  CD  GLN B 107      39.054  34.228  22.601  1.00 27.78
B    C
ATOM   1736  OE1 GLN B 107      39.453  33.093  22.852  1.00 29.49
B    O
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ATOM   1737  NE2 GLN B 107      38.613  35.056  23.539  1.00 24.76
B    N
ATOM   1738  C   GLN B 107      42.457  33.994  19.497  1.00 28.04
B    C
ATOM   1739  O   GLN B 107      42.514  32.769  19.572  1.00 28.67
B    O
ATOM   1740  N   SER B 108      43.206  34.697  18.654  1.00 29.80
B    N
ATOM   1741  CA  SER B 108      44.125  34.059  17.710  1.00 31.32
B    C
ATOM   1742  CB  SER B 108      44.873  35.129  16.917  1.00 31.54
B    C
ATOM   1743  OG  SER B 108      45.612  35.971  17.784  1.00 33.99
B    O
ATOM   1744  C   SER B 108      45.131  33.064  18.291  1.00 32.91
B    C
ATOM   1745  O   SER B 108      45.661  32.220  17.562  1.00 32.09
B    O
ATOM   1746  N   ASP B 109      45.399  33.156  19.589  1.00 33.94
B    N
ATOM   1747  CA  ASP B 109      46.346  32.243  20.221  1.00 36.43
B    C
ATOM   1748  CB  ASP B 109      47.268  33.002  21.178  1.00 38.99
B    C
ATOM   1749  CG  ASP B 109      48.429  33.660  20.464  1.00 41.54
B    C
ATOM   1750  OD1 ASP B 109      48.195  34.463  19.536  1.00 43.90
B    O
ATOM   1751  OD2 ASP B 109      49.585  33.370  20.834  1.00 45.38
B    O
ATOM   1752  C   ASP B 109      45.669  31.103  20.965  1.00 35.97
B    C
ATOM   1753  O   ASP B 109      46.340  30.261  21.558  1.00 37.38
B    O
ATOM   1754  N   ARG B 110      44.342  31.070  20.929  1.00 34.07
B    N
ATOM   1755  CA  ARG B 110      43.595  30.019  21.606  1.00 32.11
B    C
ATOM   1756  CB  ARG B 110      42.483  30.628  22.457  1.00 34.24
B    C
ATOM   1757  CG  ARG B 110      42.974  31.587  23.523  1.00 38.78
B    C
ATOM   1758  CD  ARG B 110      41.799  32.210  24.253  1.00 42.57
B    C
ATOM   1759  NE  ARG B 110      42.213  33.153  25.285  1.00 46.77
B    N
ATOM   1760  CZ  ARG B 110      42.872  32.815  26.389  1.00 48.68
B    C
ATOM   1761  NH1 ARG B 110      43.198  31.545  26.610  1.00 48.55
B    N
ATOM   1762  NH2 ARG B 110      43.197  33.750  27.274  1.00 49.15
B    N
ATOM   1763  C   ARG B 110      42.989  29.047  20.601  1.00 29.74
B    C
ATOM   1764  O   ARG B 110      43.132  29.216  19.391  1.00 28.95
B    O
ATOM   1765  N   PHE B 111      42.314  28.025  21.119  1.00 28.23
B    N
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ATOM   1766  CA  PHE B 111      41.671  27.018  20.289  1.00 25.68
B    C
ATOM   1767  CB  PHE B 111      40.429  27.619  19.627  1.00 25.02
B    C
ATOM   1768  CG  PHE B 111      39.351  28.002  20.604  1.00 21.00
B    C
ATOM   1769  CD1 PHE B 111      38.563  27.029  21.206  1.00 22.14
B    C
ATOM   1770  CD2 PHE B 111      39.151  29.331  20.954  1.00 21.84
B    C
ATOM   1771  CE1 PHE B 111      37.586  27.374  22.146  1.00 21.32
B    C
ATOM   1772  CE2 PHE B 111      38.178  29.687  21.891  1.00 22.27
B    C
ATOM   1773  CZ  PHE B 111      37.397  28.704  22.487  1.00 20.90
B    C
ATOM   1774  C   PHE B 111      42.610  26.436  19.239  1.00 25.72
B    C
ATOM   1775  O   PHE B 111      42.240  26.272  18.080  1.00 23.01
B    O
ATOM   1776  N   GLN B 112      43.829  26.119  19.659  1.00 26.79
B    N
ATOM   1777  CA  GLN B 112      44.820  25.530  18.764  1.00 28.39
B    C
ATOM   1778  CB  GLN B 112      46.211  25.622  19.392  1.00 29.98
B    C
ATOM   1779  CG  GLN B 112      46.709  27.043  19.587  1.00 33.82
B    C
ATOM   1780  CD  GLN B 112      48.085  27.100  20.227  1.00 36.64
B    C
ATOM   1781  OE1 GLN B 112      49.036  26.482  19.742  1.00 39.25
B    O
ATOM   1782  NE2 GLN B 112      48.199  27.847  21.320  1.00 36.49
B    N
ATOM   1783  C   GLN B 112      44.470  24.063  18.501  1.00 28.37
B    C
ATOM   1784  O   GLN B 112      43.903  23.389  19.358  1.00 27.65
B    O
ATOM   1785  N   PRO B 113      44.820  23.545  17.313  1.00 28.65
B    N
ATOM   1786  CD  PRO B 113      44.778  22.094  17.054  1.00 28.84
B    C
ATOM   1787  CA  PRO B 113      45.511  24.236  16.220  1.00 28.88
B    C
ATOM   1788  CB  PRO B 113      46.398  23.144  15.658  1.00 29.67
B    C
ATOM   1789  CG  PRO B 113      45.455  21.976  15.683  1.00 28.06
B    C
ATOM   1790  C   PRO B 113      44.550  24.757  15.160  1.00 29.20
B    C
ATOM   1791  O   PRO B 113      44.981  25.265  14.127  1.00 31.40
B    O
ATOM   1792  N   TYR B 114      43.253  24.624  15.414  1.00 29.48
B    N
ATOM   1793  CA  TYR B 114      42.232  25.047  14.459  1.00 29.46
B    C
ATOM   1794  CB  TYR B 114      40.839  24.695  14.992  1.00 30.23
B    C
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ATOM   1795  CG  TYR B 114      40.717  23.288  15.537  1.00 30.05
B    C
ATOM   1796  CD1 TYR B 114      40.943  22.177  14.724  1.00 32.21
B    C
ATOM   1797  CE1 TYR B 114      40.840  20.881  15.230  1.00 32.84
B    C
ATOM   1798  CD2 TYR B 114      40.383  23.069  16.871  1.00 31.34
B    C
ATOM   1799  CE2 TYR B 114      40.278  21.784  17.385  1.00 32.91
B    C
ATOM   1800  CZ  TYR B 114      40.508  20.695  16.562  1.00 33.51
B    C
ATOM   1801  OH  TYR B 114      40.413  19.424  17.081  1.00 35.76
B    O
ATOM   1802  C   TYR B 114      42.271  26.530  14.117  1.00 28.68
B    C
ATOM   1803  O   TYR B 114      42.347  26.909  12.948  1.00 29.12
B    O
ATOM   1804  N   MET B 115      42.213  27.366  15.146  1.00 28.56
B    N
ATOM   1805  CA  MET B 115      42.214  28.816  14.973  1.00 27.58
B    C
ATOM   1806  CB  MET B 115      42.343  29.488  16.344  1.00 27.94
B    C
ATOM   1807  CG  MET B 115      42.184  30.992  16.341  1.00 26.96
B    C
ATOM   1808  SD  MET B 115      40.483  31.474  16.055  1.00 27.58
B    S
ATOM   1809  CE  MET B 115      39.757  31.233  17.663  1.00 25.68
B    C
ATOM   1810  C   MET B 115      43.322  29.326  14.050  1.00 27.41
B    C
ATOM   1811  O   MET B 115      43.087  30.163  13.181  1.00 27.38
B    O
ATOM   1812  N   GLN B 116      44.530  28.814  14.240  1.00 28.20
B    N
ATOM   1813  CA  GLN B 116      45.679  29.243  13.458  1.00 29.73
B    C
ATOM   1814  CB  GLN B 116      46.935  28.565  13.997  1.00 31.41
B    C
ATOM   1815  CG  GLN B 116      47.200  28.852  15.474  1.00 34.08
B    C
ATOM   1816  CD  GLN B 116      46.074  28.388  16.390  1.00 35.14
B    C
ATOM   1817  OE1 GLN B 116      45.649  27.235  16.338  1.00 34.39
B    O
ATOM   1818  NE2 GLN B 116      45.590  29.292  17.239  1.00 37.03
B    N
ATOM   1819  C   GLN B 116      45.579  29.037  11.948  1.00 30.97
B    C
ATOM   1820  O   GLN B 116      46.279  29.697  11.184  1.00 31.99
B    O
ATOM   1821  N   GLU B 117      44.714  28.129  11.513  1.00 31.07
B    N
ATOM   1822  CA  GLU B 117      44.549  27.875  10.086  1.00 30.90
B    C
ATOM   1823  CB  GLU B 117      44.409  26.375   9.839  1.00 33.41
B    C
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ATOM   1824  CG  GLU B 117      45.624  25.581  10.273  1.00 37.00
B    C
ATOM   1825  CD  GLU B 117      45.416  24.089  10.155  1.00 39.15
B    C
ATOM   1826  OE1 GLU B 117      44.547  23.549  10.877  1.00 41.69
B    O
ATOM   1827  OE2 GLU B 117      46.123  23.460   9.339  1.00 40.83
B    O
ATOM   1828  C   GLU B 117      43.328  28.601   9.532  1.00 28.96
B    C
ATOM   1829  O   GLU B 117      43.359  29.151   8.428  1.00 29.54
B    O
ATOM   1830  N   VAL B 118      42.256  28.613  10.314  1.00 25.88
B    N
ATOM   1831  CA  VAL B 118      41.021  29.256   9.898  1.00 23.47
B    C
ATOM   1832  CB  VAL B 118      39.869  28.897  10.868  1.00 23.29
B    C
ATOM   1833  CG1 VAL B 118      38.603  29.663  10.491  1.00 21.92
B    C
ATOM   1834  CG2 VAL B 118      39.618  27.391  10.829  1.00 22.44
B    C
ATOM   1835  C   VAL B 118      41.115  30.773   9.772  1.00 22.53
B    C
ATOM   1836  O   VAL B 118      40.622  31.347   8.804  1.00 21.65
B    O
ATOM   1837  N   VAL B 119      41.748  31.429  10.739  1.00 23.10
B    N
ATOM   1838  CA  VAL B 119      41.856  32.885  10.696  1.00 23.11
B    C
ATOM   1839  CB  VAL B 119      42.573  33.432  11.941  1.00 23.48
B    C
ATOM   1840  CG1 VAL B 119      42.727  34.937  11.830  1.00 24.03
B    C
ATOM   1841  CG2 VAL B 119      41.771  33.094  13.182  1.00 25.07
B    C
ATOM   1842  C   VAL B 119      42.537  33.427   9.438  1.00 22.58
B    C
ATOM   1843  O   VAL B 119      42.025  34.350   8.805  1.00 21.65
B    O
ATOM   1844  N   PRO B 120      43.705  32.874   9.063  1.00 23.16
B    N
ATOM   1845  CD  PRO B 120      44.529  31.844   9.721  1.00 23.03
B    C
ATOM   1846  CA  PRO B 120      44.371  33.378   7.856  1.00 22.66
B    C
ATOM   1847  CB  PRO B 120      45.574  32.452   7.715  1.00 23.90
B    C
ATOM   1848  CG  PRO B 120      45.899  32.114   9.133  1.00 23.90
B    C
ATOM   1849  C   PRO B 120      43.434  33.294   6.654  1.00 23.50
B    C
ATOM   1850  O   PRO B 120      43.346  34.226   5.846  1.00 21.52
B    O
ATOM   1851  N   PHE B 121      42.727  32.169   6.555  1.00 23.36
B    N
ATOM   1852  CA  PHE B 121      41.786  31.932   5.466  1.00 22.84
B    C
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ATOM   1853  CB  PHE B 121      41.168  30.541   5.585  1.00 23.11
B    C
ATOM   1854  CG  PHE B 121      40.089  30.278   4.579  1.00 24.84
B    C
ATOM   1855  CD1 PHE B 121      40.400  30.074   3.241  1.00 25.82
B    C
ATOM   1856  CD2 PHE B 121      38.755  30.260   4.966  1.00 25.84
B    C
ATOM   1857  CE1 PHE B 121      39.396  29.856   2.302  1.00 25.59
B    C
ATOM   1858  CE2 PHE B 121      37.744  30.043   4.033  1.00 27.74
B    C
ATOM   1859  CZ  PHE B 121      38.067  29.841   2.699  1.00 26.97
B    C
ATOM   1860  C   PHE B 121      40.679  32.974   5.474  1.00 22.35
B    C
ATOM   1861  O   PHE B 121      40.382  33.572   4.443  1.00 22.39
B    O
ATOM   1862  N   LEU B 122      40.059  33.180   6.633  1.00 22.63
B    N
ATOM   1863  CA  LEU B 122      39.003  34.181   6.732  1.00 21.52
B    C
ATOM   1864  CB  LEU B 122      38.321  34.102   8.109  1.00 20.83
B    C
ATOM   1865  CG  LEU B 122      37.578  32.795   8.420  1.00 20.51
B    C
ATOM   1866  CD1 LEU B 122      36.959  32.858   9.813  1.00 19.20
B    C
ATOM   1867  CD2 LEU B 122      36.501  32.566   7.375  1.00 19.61
B    C
ATOM   1868  C   LEU B 122      39.527  35.600   6.460  1.00 21.22
B    C
ATOM   1869  O   LEU B 122      38.805  36.409   5.890  1.00 20.75
B    O
ATOM   1870  N   ALA B 123      40.771  35.878   6.853  1.00 22.05
B    N
ATOM   1871  CA  ALA B 123      41.379  37.190   6.637  1.00 24.52
B    C
ATOM   1872  CB  ALA B 123      42.804  37.224   7.280  1.00 24.63
B    C
ATOM   1873  C   ALA B 123      41.489  37.419   5.129  1.00 26.44
B    C
ATOM   1874  O   ALA B 123      41.225  38.505   4.618  1.00 25.74
B    O
ATOM   1875  N   ARG B 124      41.941  36.397   4.381  1.00 27.56
B    N
ATOM   1876  CA  ARG B 124      42.092  36.492   2.915  1.00 28.25
B    C
ATOM   1877  CB AARG B 124      42.562  35.166   2.361  0.50 31.53
B    C
ATOM   1878  CB BARG B 124      42.543  35.160   2.316  0.50 31.52
B    C
ATOM   1879  CG AARG B 124      43.971  34.730   2.819  0.50 34.27
B    C
ATOM   1880  CG BARG B 124      43.953  34.764   2.660  0.50 34.62
B    C
ATOM   1881  CD AARG B 124      44.500  33.566   1.961  0.50 36.72
B    C
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ATOM   1882  CD BARG B 124      44.485  33.793   1.624  0.50 36.96
B    C
ATOM   1883  NE AARG B 124      44.367  32.250   2.587  0.50 38.21
B    N
ATOM   1884  NE BARG B 124      43.633  32.620   1.416  0.50 39.16
B    N
ATOM   1885  CZ AARG B 124      45.302  31.685   3.346  0.50 39.41
B    C
ATOM   1886  CZ BARG B 124      42.571  32.573   0.613  0.50 39.85
B    C
ATOM   1887  NH1AARG B 124      46.444  32.318   3.574  0.50 39.45
B    N
ATOM   1888  NH1BARG B 124      42.196  33.638  -0.084  0.50 39.88
B    N
ATOM   1889  NH2AARG B 124      45.097  30.487   3.874  0.50 40.70
B    N
ATOM   1890  NH2BARG B 124      41.878  31.449   0.504  0.50 40.63
B    N
ATOM   1891  C   ARG B 124      40.755  36.861   2.270  1.00 28.59
B    C
ATOM   1892  O   ARG B 124      40.699  37.698   1.347  1.00 28.10
B    O
ATOM   1893  N   LEU B 125      39.685  36.193   2.734  1.00 28.01
B    N
ATOM   1894  CA  LEU B 125      38.367  36.466   2.203  1.00 25.98
B    C
ATOM   1895  CB  LEU B 125      37.333  35.525   2.822  1.00 27.46
B    C
ATOM   1896  CG  LEU B 125      37.385  34.019   2.530  1.00 27.82
B    C
ATOM   1897  CD1 LEU B 125      36.107  33.354   3.052  1.00 26.92
B    C
ATOM   1898  CD2 LEU B 125      37.519  33.771   1.039  1.00 27.76
B    C
ATOM   1899  C   LEU B 125      37.940  37.905   2.469  1.00 25.43
B    C
ATOM   1900  O   LEU B 125      37.301  38.547   1.629  1.00 25.94
B    O
ATOM   1901  N   SER B 126      38.262  38.392   3.660  1.00 24.59
B    N
ATOM   1902  CA  SER B 126      37.937  39.757   4.040  1.00 25.45
B    C
ATOM   1903  CB  SER B 126      38.427  40.030   5.463  1.00 25.70
B    C
ATOM   1904  OG  SER B 126      38.216  41.382   5.819  1.00 24.65
B    O
ATOM   1905  C   SER B 126      38.671  40.668   3.067  1.00 26.58
B    C
ATOM   1906  O   SER B 126      38.126  41.664   2.584  1.00 25.56
B    O
ATOM   1907  N   ASN B 127      39.920  40.311   2.789  1.00 28.53
B    N
ATOM   1908  CA  ASN B 127      40.766  41.069   1.875  1.00 31.42
B    C
ATOM   1909  CB  ASN B 127      42.149  40.415   1.810  1.00 33.56
B    C
ATOM   1910  CG  ASN B 127      43.145  41.230   1.017  1.00 37.76
B    C
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ATOM   1911  OD1 ASN B 127      43.392  42.396   1.326  1.00 41.52
B    O
ATOM   1912  ND2 ASN B 127      43.734  40.617  -0.008  1.00 37.74
B    N
ATOM   1913  C   ASN B 127      40.114  41.110   0.492  1.00 31.83
B    C
ATOM   1914  O   ASN B 127      40.081  42.154  -0.160  1.00 32.67
B    O
ATOM   1915  N   ARG B 128      39.584  39.971   0.057  1.00 33.16
B    N
ATOM   1916  CA  ARG B 128      38.919  39.872  -1.239  1.00 35.03
B    C
ATOM   1917  CB  ARG B 128      38.477  38.429  -1.499  1.00 37.42
B    C
ATOM   1918  CG  ARG B 128      39.572  37.384  -1.393  1.00 40.66
B    C
ATOM   1919  CD  ARG B 128      40.484  37.388  -2.602  1.00 44.62
B    C
ATOM   1920  NE  ARG B 128      41.399  36.248  -2.596  1.00 47.25
B    N
ATOM   1921  CZ  ARG B 128      42.370  36.069  -1.706  1.00 49.09
B    C
ATOM   1922  NH1 ARG B 128      42.562  36.957  -0.737  1.00 49.49
B    N
ATOM   1923  NH2 ARG B 128      43.155  35.002  -1.787  1.00 49.90
B    N
ATOM   1924  C   ARG B 128      37.686  40.780  -1.311  1.00 35.69
B    C
ATOM   1925  O   ARG B 128      37.401  41.370  -2.352  1.00 35.80
B    O
ATOM   1926  N   LEU B 129      36.955  40.886  -0.206  1.00 35.75
B    N
ATOM   1927  CA  LEU B 129      35.746  41.709  -0.161  1.00 36.71
B    C
ATOM   1928  CB  LEU B 129      34.816  41.213   0.952  1.00 35.61
B    C
ATOM   1929  CG  LEU B 129      34.227  39.810   0.784  1.00 36.13
B    C
ATOM   1930  CD1 LEU B 129      33.424  39.445   2.017  1.00 35.68
B    C
ATOM   1931  CD2 LEU B 129      33.344  39.761  -0.454  1.00 34.32
B    C
ATOM   1932  C   LEU B 129      36.018  43.200   0.043  1.00 37.24
B    C
ATOM   1933  O   LEU B 129      35.086  43.989   0.178  1.00 37.30
B    O
ATOM   1934  N   SER B 130      37.291  43.577   0.059  1.00 39.20
B    N
ATOM   1935  CA  SER B 130      37.693  44.969   0.268  1.00 41.51
B    C
ATOM   1936  CB  SER B 130      39.122  45.191  -0.238  1.00 41.64
B    C
ATOM   1937  OG  SER B 130      40.062  44.614   0.651  1.00 44.96
B    O
ATOM   1938  C   SER B 130      36.789  46.030  -0.345  1.00 41.71
B    C
ATOM   1939  O   SER B 130      36.579  46.056  -1.550  1.00 43.01
B    O
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ATOM 1940 N THR B 131 36.259 46.900 0.508 1.00 42.65
B N
ATOM 1941 CA THR B 131 35.399 48.012 0.103 1.00 43.65
B C
ATOM 1942 CB THR B 131 36.223 49.110 -0.617 1.00 44.32
B C
ATOM 1943 OG1 THR B 131 36.682 48.620 -1.885 1.00 45.77
B O
ATOM 1944 CG2 THR B 131 37.428 49.511 0.236 1.00 44.02
B C
ATOM 1945 C THR B 131 34.161 47.723 -0.747 1.00 43.82
B C
ATOM 1946 O THR B 131 33.401 48.649 -1.041 1.00 43.74
B O
ATOM 1947 N CYS B 132 33.945 46.470 -1.146 1.00 43.43
B N
ATOM 1948 CA CYS B 132 32.762 46.157 -1.949 1.00 42.56
B C
ATOM 1949 C CYS B 132 31.564 46.639 -1.146 1.00 42.53
B C
ATOM 1950 O CYS B 132 31.515 46.452 0.068 1.00 42.41
B O
ATOM 1951 CB CYS B 132 32.644 44.651 -2.205 1.00 41.08
B C
ATOM 1952 SG CYS B 132 32.191 43.674 -0.738 1.00 40.07
B S
ATOM 1953 N HIS B 133 30.608 47.277 -1.813 1.00 44.03
B N
ATOM 1954 CA HIS B 133 29.434 47.790 -1.120 1.00 45.92
B C
ATOM 1955 CB HIS B 133 29.661 49.247 -0.723 1.00 48.01
B C
ATOM 1956 CG HIS B 133 29.999 50.136 -1.877 1.00 50.95
B C
ATOM 1957 CD2 HIS B 133 29.344 51.195 -2.408 1.00 51.52
B C
ATOM 1958 ND1 HIS B 133 31.132 49.961 -2.642 1.00 52.14
B N
ATOM 1959 CE1 HIS B 133 31.161 50.875 -3.596 1.00 52.81
B C
ATOM 1960 NE2 HIS B 133 30.088 51.636 -3.477 1.00 52.91
B N
ATOM 1961 C HIS B 133 28.158 47.680 -1.940 1.00 45.88
B C
ATOM 1962 O HIS B 133 28.143 47.067 -3.005 1.00 45.95
B O
ATOM 1963 N ILE B 134 27.086 48.281 -1.433 1.00 46.79
B N
ATOM 1964 CA ILE B 134 25.798 48.245 -2.110 1.00 48.22
B C
ATOM 1965 CB ILE B 134 24.686 47.725 -1.172 1.00 47.47
B C
ATOM 1966 CG2 ILE B 134 25.035 46.328 -0.684 1.00 47.42
B C
ATOM 1967 CG1 ILE B 134 24.515 48.672 0.016 1.00 46.57
B C
ATOM 1968 CD ILE B 134 23.426 48.248 0.977 1.00 47.17
B C

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ATOM   1969  C   ILE B 134      25.385  49.614  -2.644  1.00 49.84
B    C
ATOM   1970  O   ILE B 134      26.079  50.611  -2.439  1.00 49.80
B    O
ATOM   1971  N   GLU B 135      24.243  49.642  -3.326  1.00 50.44
B    N
ATOM   1972  CA  GLU B 135      23.700  50.860  -3.921  1.00 51.87
B    C
ATOM   1973  CB  GLU B 135      22.405  50.531  -4.671  1.00 53.19
B    C
ATOM   1974  CG  GLU B 135      22.597  49.598  -5.859  1.00 55.61
B    C
ATOM   1975  CD  GLU B 135      23.283  48.298  -5.475  1.00 57.90
B    C
ATOM   1976  OE1 GLU B 135      22.787  47.613  -4.554  1.00 58.58
B    O
ATOM   1977  OE2 GLU B 135      24.317  47.963  -6.093  1.00 59.79
B    O
ATOM   1978  C   GLU B 135      23.445  51.989  -2.918  1.00 51.36
B    C
ATOM   1979  O   GLU B 135      24.324  52.820  -2.677  1.00 51.02
B    O
ATOM   1980  N   GLY B 136      22.245  52.022  -2.341  1.00 50.44
B    N
ATOM   1981  CA  GLY B 136      21.930  53.074  -1.393  1.00 49.30
B    C
ATOM   1982  C   GLY B 136      21.197  52.672  -0.128  1.00 47.53
B    C
ATOM   1983  O   GLY B 136      20.289  51.839  -0.147  1.00 46.93
B    O
ATOM   1984  N   ASP B 137      21.614  53.284   0.976  1.00 46.58
B    N
ATOM   1985  CA  ASP B 137      21.027  53.064   2.293  1.00 45.28
B    C
ATOM   1986  CB  ASP B 137      19.559  53.486   2.277  1.00 47.28
B    C
ATOM   1987  CG  ASP B 137      18.981  53.623   3.661  1.00 48.41
B    C
ATOM   1988  OD1 ASP B 137      19.131  52.681   4.465  1.00 48.28
B    O
ATOM   1989  OD2 ASP B 137      18.378  54.675   3.947  1.00 51.40
B    O
ATOM   1990  C   ASP B 137      21.133  51.650   2.844  1.00 43.55
B    C
ATOM   1991  O   ASP B 137      20.277  50.803   2.590  1.00 43.30
B    O
ATOM   1992  N   ASP B 138      22.184  51.416   3.620  1.00 40.92
B    N
ATOM   1993  CA  ASP B 138      22.419  50.118   4.237  1.00 38.17
B    C
ATOM   1994  CB  ASP B 138      23.899  49.774   4.155  1.00 37.09
B    C
ATOM   1995  CG  ASP B 138      24.751  50.703   4.992  1.00 38.19
B    C
ATOM   1996  OD1 ASP B 138      24.292  51.828   5.283  1.00 38.67
B    O
ATOM   1997  OD2 ASP B 138      25.882  50.319   5.354  1.00 39.46
B    O
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ATOM   1998  C   ASP B 138      21.988  50.124   5.712  1.00 36.48
B    C
ATOM   1999  O   ASP B 138      22.428  49.286   6.501  1.00 36.23
B    O
ATOM   2000  N   LEU B 139      21.124  51.065   6.076  1.00 35.08
B    N
ATOM   2001  CA  LEU B 139      20.650  51.196   7.450  1.00 33.13
B    C
ATOM   2002  CB  LEU B 139      19.592  52.298   7.533  1.00 36.06
B    C
ATOM   2003  CG  LEU B 139      19.099  52.661   8.934  1.00 37.59
B    C
ATOM   2004  CD1 LEU B 139      20.224  53.321   9.706  1.00 39.27
B    C
ATOM   2005  CD2 LEU B 139      17.909  53.599   8.840  1.00 40.35
B    C
ATOM   2006  C   LEU B 139      20.087  49.903   8.030  1.00 31.75
B    C
ATOM   2007  O   LEU B 139      20.423  49.524   9.153  1.00 31.56
B    O
ATOM   2008  N   HIS B 140      19.227  49.226   7.275  1.00 29.29
B    N
ATOM   2009  CA  HIS B 140      18.634  47.975   7.748  1.00 27.87
B    C
ATOM   2010  CB  HIS B 140      17.598  47.465   6.738  1.00 29.34
B    C
ATOM   2011  CG  HIS B 140      18.158  47.209   5.374  1.00 30.92
B    C
ATOM   2012  CD2 HIS B 140      18.179  46.088   4.614  1.00 32.52
B    C
ATOM   2013  ND1 HIS B 140      18.796  48.183   4.636  1.00 33.09
B    N
ATOM   2014  CE1 HIS B 140      19.187  47.672   3.481  1.00 33.64
B    C
ATOM   2015  NE2 HIS B 140      18.826  46.403   3.442  1.00 33.59
B    N
ATOM   2016  C   HIS B 140      19.714  46.912   7.977  1.00 24.95
B    C
ATOM   2017  O   HIS B 140      19.614  46.083   8.878  1.00 24.47
B    O
ATOM   2018  N   ILE B 141      20.752  46.946   7.156  1.00 23.58
B    N
ATOM   2019  CA  ILE B 141      21.840  45.991   7.289  1.00 22.50
B    C
ATOM   2020  CB  ILE B 141      22.765  46.043   6.059  1.00 23.20
B    C
ATOM   2021  CG2 ILE B 141      23.982  45.171   6.283  1.00 22.62
B    C
ATOM   2022  CG1 ILE B 141      21.983  45.592   4.818  1.00 24.14
B    C
ATOM   2023  CD  ILE B 141      22.783  45.609   3.541  1.00 26.45
B    C
ATOM   2024  C   ILE B 141      22.641  46.287   8.556  1.00 22.44
B    C
ATOM   2025  O   ILE B 141      22.899  45.390   9.361  1.00 19.54
B    O
ATOM   2026  N   GLN B 142      23.020  47.548   8.738  1.00 21.44
B    N
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ATOM   2027  CA  GLN B 142      23.792  47.932   9.913  1.00 20.93
B    C
ATOM   2028  CB  GLN B 142      24.152  49.418   9.858  1.00 23.51
B    C
ATOM   2029  CG  GLN B 142      25.108  49.807   8.734  1.00 27.67
B    C
ATOM   2030  CD  GLN B 142      26.345  48.920   8.666  1.00 31.25
B    C
ATOM   2031  OE1 GLN B 142      26.874  48.488   9.692  1.00 33.98
B    O
ATOM   2032  NE2 GLN B 142      26.819  48.659   7.451  1.00 31.45
B    N
ATOM   2033  C   GLN B 142      23.031  47.634  11.202  1.00 19.58
B    C
ATOM   2034  O   GLN B 142      23.621  47.216  12.195  1.00 19.52
B    O
ATOM   2035  N   ARG B 143      21.718  47.847  11.182  1.00 19.46
B    N
ATOM   2036  CA  ARG B 143      20.891  47.598  12.355  1.00 18.97
B    C
ATOM   2037  CB  ARG B 143      19.454  48.084  12.117  1.00 19.80
B    C
ATOM   2038  CG  ARG B 143      18.572  47.982  13.361  1.00 20.29
B    C
ATOM   2039  CD  ARG B 143      17.151  48.457  13.118  1.00 24.78
B    C
ATOM   2040  NE  ARG B 143      17.081  49.859  12.703  1.00 27.22
B    N
ATOM   2041  CZ  ARG B 143      16.831  50.261  11.459  1.00 29.43
B    C
ATOM   2042  NH1 ARG B 143      16.625  49.367  10.499  1.00 28.10
B    N
ATOM   2043  NH2 ARG B 143      16.785  51.557  11.172  1.00 29.11
B    N
ATOM   2044  C   ARG B 143      20.879  46.116  12.716  1.00 19.02
B    C
ATOM   2045  O   ARG B 143      20.936  45.751  13.896  1.00 18.36
B    O
ATOM   2046  N   ASN B 144      20.795  45.259  11.703  1.00 17.05
B    N
ATOM   2047  CA  ASN B 144      20.783  43.822  11.944  1.00 17.50
B    C
ATOM   2048  CB  ASN B 144      20.492  43.053  10.649  1.00 16.62
B    C
ATOM   2049  CG  ASN B 144      19.062  43.240  10.169  1.00 18.56
B    C
ATOM   2050  OD1 ASN B 144      18.280  43.963  10.781  1.00 15.87
B    O
ATOM   2051  ND2 ASN B 144      18.714  42.582   9.070  1.00 18.04
B    N
ATOM   2052  C   ASN B 144      22.125  43.381  12.503  1.00 16.92
B    C
ATOM   2053  O   ASN B 144      22.181  42.547  13.400  1.00 16.92
B    O
ATOM   2054  N   VAL B 145      23.205  43.943  11.967  1.00 15.33
B    N
ATOM   2055  CA  VAL B 145      24.544  43.598  12.423  1.00 15.98
B    C
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ATOM   2056  CB  VAL B 145      25.615  44.191  11.469  1.00 17.14
B    C
ATOM   2057  CG1 VAL B 145      27.020  43.920  12.007  1.00 17.91
B    C
ATOM   2058  CG2 VAL B 145      25.456  43.584  10.080  1.00 18.98
B    C
ATOM   2059  C   VAL B 145      24.760  44.118  13.846  1.00 16.15
B    C
ATOM   2060  O   VAL B 145      25.396  43.454  14.672  1.00 13.69
B    O
ATOM   2061  N   GLN B 146      24.221  45.302  14.134  1.00 14.53
B    N
ATOM   2062  CA  GLN B 146      24.359  45.893  15.464  1.00 12.59
B    C
ATOM   2063  CB  GLN B 146      23.598  47.222  15.546  1.00 12.98
B    C
ATOM   2064  CG  GLN B 146      23.739  47.970  16.885  1.00 15.51
B    C
ATOM   2065  CD  GLN B 146      25.100  48.641  17.058  1.00 18.34
B    C
ATOM   2066  OE1 GLN B 146      25.593  49.306  16.148  1.00 17.29
B    O
ATOM   2067  NE2 GLN B 146      25.700  48.483  18.233  1.00 19.22
B    N
ATOM   2068  C   GLN B 146      23.814  44.926  16.516  1.00 13.75
B    C
ATOM   2069  O   GLN B 146      24.388  44.778  17.592  1.00 11.09
B    O
ATOM   2070  N   LYS B 147      22.703  44.267  16.205  1.00 14.74
B    N
ATOM   2071  CA  LYS B 147      22.112  43.326  17.147  1.00 15.33
B    C
ATOM   2072  CB  LYS B 147      20.820  42.737  16.575  1.00 19.41
B    C
ATOM   2073  CG  LYS B 147      19.632  43.681  16.657  1.00 24.48
B    C
ATOM   2074  CD  LYS B 147      18.351  43.003  16.173  1.00 27.59
B    C
ATOM   2075  CE  LYS B 147      17.113  43.791  16.583  1.00 30.10
B    C
ATOM   2076  NZ  LYS B 147      17.197  45.226  16.199  1.00 32.34
B    N
ATOM   2077  C   LYS B 147      23.075  42.202  17.488  1.00 14.99
B    C
ATOM   2078  O   LYS B 147      23.242  41.851  18.656  1.00 13.88
B    O
ATOM   2079  N   LEU B 148      23.698  41.630  16.463  1.00 13.47
B    N
ATOM   2080  CA  LEU B 148      24.646  40.546  16.664  1.00 11.96
B    C
ATOM   2081  CB  LEU B 148      25.128  40.020  15.309  1.00 11.28
B    C
ATOM   2082  CG  LEU B 148      26.174  38.901  15.273  1.00 13.54
B    C
ATOM   2083  CD1 LEU B 148      26.101  38.200  13.936  1.00 12.19
B    C
ATOM   2084  CD2 LEU B 148      27.561  39.466  15.516  1.00 12.71
B    C
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ATOM   2085  C   LEU B 148      25.818  41.072  17.486  1.00 12.75
B    C
ATOM   2086  O   LEU B 148      26.256  40.428  18.434  1.00 13.22
B    O
ATOM   2087  N   LYS B 149      26.309  42.254  17.121  1.00 12.62
B    N
ATOM   2088  CA  LYS B 149      27.423  42.886  17.818  1.00 13.95
B    C
ATOM   2089  CB  LYS B 149      27.794  44.203  17.124  1.00 13.88
B    C
ATOM   2090  CG  LYS B 149      28.555  43.999  15.828  1.00 17.34
B    C
ATOM   2091  CD  LYS B 149      28.430  45.170  14.872  1.00 22.47
B    C
ATOM   2092  CE  LYS B 149      28.881  46.482  15.472  1.00 25.42
B    C
ATOM   2093  NZ  LYS B 149      29.064  47.513  14.402  1.00 24.53
B    N
ATOM   2094  C   LYS B 149      27.122  43.137  19.293  1.00 14.22
B    C
ATOM   2095  O   LYS B 149      27.956  42.850  20.151  1.00 15.40
B    O
ATOM   2096  N   ASP B 150      25.939  43.663  19.593  1.00 13.64
B    N
ATOM   2097  CA  ASP B 150      25.576  43.928  20.988  1.00 13.95
B    C
ATOM   2098  CB  ASP B 150      24.198  44.589  21.080  1.00 15.50
B    C
ATOM   2099  CG  ASP B 150      24.172  45.985  20.493  1.00 16.66
B    C
ATOM   2100  OD1 ASP B 150      25.253  46.586  20.324  1.00 16.66
B    O
ATOM   2101  OD2 ASP B 150      23.055  46.480  20.212  1.00 19.61
B    O
ATOM   2102  C   ASP B 150      25.554  42.661  21.843  1.00 13.62
B    C
ATOM   2103  O   ASP B 150      25.986  42.655  23.002  1.00 12.88
B    O
ATOM   2104  N   THR B 151      25.017  41.591  21.276  1.00 12.91
B    N
ATOM   2105  CA  THR B 151      24.926  40.326  21.988  1.00 14.27
B    C
ATOM   2106  CB  THR B 151      24.211  39.278  21.127  1.00 16.02
B    C
ATOM   2107  OG1 THR B 151      22.904  39.763  20.802  1.00 15.49
B    O
ATOM   2108  CG2 THR B 151      24.101  37.951  21.862  1.00 15.10
B    C
ATOM   2109  C   THR B 151      26.313  39.830  22.340  1.00 14.06
B    C
ATOM   2110  O   THR B 151      26.554  39.381  23.460  1.00 15.38
B    O
ATOM   2111  N   VAL B 152      27.231  39.915  21.383  1.00 12.61
B    N
ATOM   2112  CA  VAL B 152      28.594  39.469  21.621  1.00 13.27
B    C
ATOM   2113  CB  VAL B 152      29.429  39.499  20.321  1.00 13.23
B    C
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ATOM   2114  CG1 VAL B 152      30.900  39.371  20.647  1.00 12.74
B    C
ATOM   2115  CG2 VAL B 152      29.001  38.354  19.409  1.00 13.59
B    C
ATOM   2116  C   VAL B 152      29.283  40.335  22.672  1.00 12.43
B    C
ATOM   2117  O   VAL B 152      29.916  39.817  23.587  1.00 13.68
B    O
ATOM   2118  N   LYS B 153      29.141  41.653  22.549  1.00 11.31
B    N
ATOM   2119  CA  LYS B 153      29.786  42.570  23.489  1.00  9.49
B    C
ATOM   2120  CB  LYS B 153      29.720  44.011  22.965  1.00  9.07
B    C
ATOM   2121  CG  LYS B 153      30.559  44.253  21.708  1.00  7.62
B    C
ATOM   2122  CD  LYS B 153      32.027  43.864  21.936  1.00  9.41
B    C
ATOM   2123  CE  LYS B 153      32.891  44.041  20.688  1.00  9.65
B    C
ATOM   2124  NZ  LYS B 153      34.308  43.621  20.957  1.00  8.41
B    N
ATOM   2125  C   LYS B 153      29.231  42.505  24.902  1.00  9.60
B    C
ATOM   2126  O   LYS B 153      29.990  42.550  25.872  1.00 10.58
B    O
ATOM   2127  N   LYS B 154      27.917  42.398  25.034  1.00 10.82
B    N
ATOM   2128  CA  LYS B 154      27.318  42.330  26.362  1.00 12.31
B    C
ATOM   2129  CB  LYS B 154      25.787  42.296  26.255  1.00 14.53
B    C
ATOM   2130  CG  LYS B 154      25.109  41.913  27.561  1.00 20.06
B    C
ATOM   2131  CD  LYS B 154      23.589  42.030  27.501  1.00 24.39
B    C
ATOM   2132  CE  LYS B 154      22.991  41.812  28.891  1.00 24.64
B    C
ATOM   2133  NZ  LYS B 154      21.499  41.697  28.874  1.00 27.27
B    N
ATOM   2134  C   LYS B 154      27.808  41.105  27.138  1.00 14.73
B    C
ATOM   2135  O   LYS B 154      27.940  41.141  28.366  1.00 13.45
B    O
ATOM   2136  N   LEU B 155      28.090  40.026  26.412  1.00 14.59
B    N
ATOM   2137  CA  LEU B 155      28.546  38.783  27.024  1.00 15.48
B    C
ATOM   2138  CB  LEU B 155      28.120  37.596  26.156  1.00 14.97
B    C
ATOM   2139  CG  LEU B 155      26.614  37.319  26.219  1.00 16.78
B    C
ATOM   2140  CD1 LEU B 155      26.251  36.184  25.283  1.00 17.88
B    C
ATOM   2141  CD2 LEU B 155      26.233  36.976  27.659  1.00 18.88
B    C
ATOM   2142  C   LEU B 155      30.043  38.710  27.305  1.00 16.52
B    C
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ATOM   2143  O   LEU B 155      30.522  37.749  27.904  1.00 16.70
B    O
ATOM   2144  N   GLY B 156      30.788  39.723  26.878  1.00 16.38
B    N
ATOM   2145  CA  GLY B 156      32.213  39.716  27.146  1.00 17.98
B    C
ATOM   2146  C   GLY B 156      32.918  38.521  26.542  1.00 18.96
B    C
ATOM   2147  O   GLY B 156      32.658  38.159  25.398  1.00 19.62
B    O
ATOM   2148  N   GLU B 157      33.807  37.897  27.305  1.00 20.01
B    N
ATOM   2149  CA  GLU B 157      34.547  36.751  26.790  1.00 22.65
B    C
ATOM   2150  CB  GLU B 157      35.504  36.198  27.844  1.00 26.57
B    C
ATOM   2151  CG  GLU B 157      36.377  35.060  27.323  1.00 32.56
B    C
ATOM   2152  CD  GLU B 157      37.622  34.860  28.160  1.00 36.42
B    C
ATOM   2153  OE1 GLU B 157      37.487  34.500  29.348  1.00 39.12
B    O
ATOM   2154  OE2 GLU B 157      38.738  35.071  27.632  1.00 40.09
B    O
ATOM   2155  C   GLU B 157      33.642  35.628  26.304  1.00 21.05
B    C
ATOM   2156  O   GLU B 157      33.940  34.972  25.309  1.00 19.94
B    O
ATOM   2157  N   SER B 158      32.551  35.395  27.025  1.00 20.79
B    N
ATOM   2158  CA  SER B 158      31.602  34.357  26.650  1.00 20.47
B    C
ATOM   2159  CB  SER B 158      30.481  34.264  27.684  1.00 21.91
B    C
ATOM   2160  OG  SER B 158      31.000  33.902  28.948  1.00 26.50
B    O
ATOM   2161  C   SER B 158      31.006  34.696  25.291  1.00 19.88
B    C
ATOM   2162  O   SER B 158      30.649  33.803  24.519  1.00 20.24
B    O
ATOM   2163  N   GLY B 159      30.890  35.991  25.010  1.00 18.62
B    N
ATOM   2164  CA  GLY B 159      30.343  36.426  23.733  1.00 17.19
B    C
ATOM   2165  C   GLY B 159      31.272  36.008  22.611  1.00 15.21
B    C
ATOM   2166  O   GLY B 159      30.828  35.574  21.536  1.00 13.42
B    O
ATOM   2167  N   GLU B 160      32.569  36.138  22.862  1.00 12.99
B    N
ATOM   2168  CA  GLU B 160      33.571  35.759  21.880  1.00 15.94
B    C
ATOM   2169  CB  GLU B 160      34.963  36.197  22.349  1.00 18.02
B    C
ATOM   2170  CG  GLU B 160      35.143  37.708  22.329  1.00 21.23
B    C
ATOM   2171  CD  GLU B 160      36.471  38.151  22.913  1.00 25.05
B    C
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ATOM   2172  OE1 GLU B 160      37.519  37.597  22.522  1.00 26.71
B    O
ATOM   2173  OE2 GLU B 160      36.467  39.065  23.758  1.00 26.22
B    O
ATOM   2174  C   GLU B 160      33.533  34.252  21.646  1.00 16.05
B    C
ATOM   2175  O   GLU B 160      33.584  33.791  20.503  1.00 16.68
B    O
ATOM   2176  N   ILE B 161      33.430  33.489  22.728  1.00 15.72
B    N
ATOM   2177  CA  ILE B 161      33.380  32.033  22.628  1.00 15.75
B    C
ATOM   2178  CB AILE B 161      33.334  31.371  24.025  0.50 17.43
B    C
ATOM   2179  CB BILE B 161      33.345  31.389  24.043  0.50 17.65
B    C
ATOM   2180  CG2AILE B 161      33.225  29.860  23.887  0.50 18.33
B    C
ATOM   2181  CG2BILE B 161      33.204  29.879  23.924  0.50 18.35
B    C
ATOM   2182  CG1AILE B 161      34.588  31.753  24.820  0.50 18.68
B    C
ATOM   2183  CG1BILE B 161      34.627  31.750  24.803  0.50 18.95
B    C
ATOM   2184  CD AILE B 161      35.890  31.386  24.139  0.50 18.08
B    C
ATOM   2185  CD BILE B 161      34.640  31.314  26.252  0.50 19.38
B    C
ATOM   2186  C   ILE B 161      32.151  31.616  21.828  1.00 15.04
B    C
ATOM   2187  O   ILE B 161      32.233  30.745  20.960  1.00 13.38
B    O
ATOM   2188  N   LYS B 162      31.017  32.251  22.110  1.00 14.57
B    N
ATOM   2189  CA  LYS B 162      29.782  31.938  21.401  1.00 14.05
B    C
ATOM   2190  CB  LYS B 162      28.621  32.771  21.954  1.00 14.23
B    C
ATOM   2191  CG  LYS B 162      27.299  32.559  21.206  1.00 15.87
B    C
ATOM   2192  CD  LYS B 162      26.211  33.520  21.678  1.00 16.15
B    C
ATOM   2193  CE  LYS B 162      25.913  33.359  23.163  1.00 18.43
B    C
ATOM   2194  NZ  LYS B 162      25.341  32.018  23.490  1.00 22.02
B    N
ATOM   2195  C   LYS B 162      29.933  32.208  19.910  1.00 12.51
B    C
ATOM   2196  O   LYS B 162      29.445  31.442  19.078  1.00 13.34
B    O
ATOM   2197  N   ALA B 163      30.611  33.297  19.574  1.00 12.30
B    N
ATOM   2198  CA  ALA B 163      30.822  33.656  18.177  1.00 12.59
B    C
ATOM   2199  CB  ALA B 163      31.474  35.036  18.089  1.00 12.94
B    C
ATOM   2200  C   ALA B 163      31.684  32.617  17.454  1.00 12.63
B    C
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ATOM   2201  O   ALA B 163      31.435  32.281  16.293  1.00 13.56
B    O
ATOM   2202  N   ILE B 164      32.704  32.111  18.135  1.00 13.23
B    N
ATOM   2203  CA  ILE B 164      33.578  31.107  17.532  1.00 10.59
B    C
ATOM   2204  CB  ILE B 164      34.824  30.853  18.403  1.00 12.38
B    C
ATOM   2205  CG2 ILE B 164      35.701  29.767  17.768  1.00  8.98
B    C
ATOM   2206  CG1 ILE B 164      35.617  32.155  18.566  1.00  9.24
B    C
ATOM   2207  CD  ILE B 164      36.746  32.058  19.590  1.00 11.68
B    C
ATOM   2208  C   ILE B 164      32.793  29.804  17.379  1.00 12.14
B    C
ATOM   2209  O   ILE B 164      33.009  29.049  16.431  1.00 12.85
B    O
ATOM   2210  N   GLY B 165      31.868  29.558  18.305  1.00 10.88
B    N
ATOM   2211  CA  GLY B 165      31.063  28.345  18.252  1.00 13.41
B    C
ATOM   2212  C   GLY B 165      30.109  28.337  17.072  1.00 14.68
B    C
ATOM   2213  O   GLY B 165      29.583  27.290  16.686  1.00 14.73
B    O
ATOM   2214  N   GLU B 166      29.890  29.512  16.495  1.00 13.01
B    N
ATOM   2215  CA  GLU B 166      29.011  29.656  15.349  1.00 14.06
B    C
ATOM   2216  CB  GLU B 166      28.031  30.773  15.621  1.00 16.63
B    C
ATOM   2217  CG  GLU B 166      27.344  30.594  16.942  1.00 21.35
B    C
ATOM   2218  CD  GLU B 166      26.278  29.510  16.908  1.00 25.81
B    C
ATOM   2219  OE1 GLU B 166      26.648  28.326  16.873  1.00 31.72
B    O
ATOM   2220  OE2 GLU B 166      25.065  29.822  16.913  1.00 30.04
B    O
ATOM   2221  C   GLU B 166      29.767  29.952  14.062  1.00 11.84
B    C
ATOM   2222  O   GLU B 166      29.164  30.323  13.054  1.00 11.51
B    O
ATOM   2223  N   LEU B 167      31.084  29.781  14.090  1.00 10.92
B    N
ATOM   2224  CA  LEU B 167      31.895  30.033  12.903  1.00 12.37
B    C
ATOM   2225  CB  LEU B 167      33.391  29.836  13.195  1.00 15.29
B    C
ATOM   2226  CG  LEU B 167      34.115  31.001  13.872  1.00 20.06
B    C
ATOM   2227  CD1 LEU B 167      35.562  30.612  14.125  1.00 22.06
B    C
ATOM   2228  CD2 LEU B 167      34.033  32.247  12.996  1.00 20.29
B    C
ATOM   2229  C   LEU B 167      31.496  29.137  11.739  1.00 13.10
B    C
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ATOM   2230  O   LEU B 167      31.733  29.481  10.585  1.00 12.57
B    O
ATOM   2231  N   ASP B 168      30.901  27.986  12.034  1.00 12.74
B    N
ATOM   2232  CA  ASP B 168      30.478  27.100  10.960  1.00 14.28
B    C
ATOM   2233  CB  ASP B 168      30.058  25.727  11.515  1.00 13.57
B    C
ATOM   2234  CG  ASP B 168      29.185  25.821  12.760  1.00 17.07
B    C
ATOM   2235  OD1 ASP B 168      28.964  26.930  13.295  1.00 14.89
B    O
ATOM   2236  OD2 ASP B 168      28.723  24.755  13.218  1.00 18.76
B    O
ATOM   2237  C   ASP B 168      29.335  27.767  10.186  1.00 12.65
B    C
ATOM   2238  O   ASP B 168      29.312  27.747   8.958  1.00 13.63
B    O
ATOM   2239  N   LEU B 169      28.403  28.379  10.903  1.00 11.65
B    N
ATOM   2240  CA  LEU B 169      27.293  29.068  10.255  1.00 14.38
B    C
ATOM   2241  CB  LEU B 169      26.245  29.481  11.283  1.00 15.94
B    C
ATOM   2242  CG  LEU B 169      25.462  28.363  11.971  1.00 18.22
B    C
ATOM   2243  CD1 LEU B 169      24.391  28.973  12.880  1.00 18.16
B    C
ATOM   2244  CD2 LEU B 169      24.822  27.472  10.913  1.00 20.52
B    C
ATOM   2245  C   LEU B 169      27.791  30.311   9.520  1.00 15.25
B    C
ATOM   2246  O   LEU B 169      27.249  30.701   8.483  1.00 14.55
B    O
ATOM   2247  N   LEU B 170      28.821  30.944  10.062  1.00 15.29
B    N
ATOM   2248  CA  LEU B 170      29.359  32.133   9.421  1.00 16.17
B    C
ATOM   2249  CB  LEU B 170      30.418  32.795  10.309  1.00 16.47
B    C
ATOM   2250  CG  LEU B 170      31.234  33.908   9.639  1.00 18.75
B    C
ATOM   2251  CD1 LEU B 170      30.309  34.997   9.152  1.00 20.23
B    C
ATOM   2252  CD2 LEU B 170      32.242  34.479  10.622  1.00 20.78
B    C
ATOM   2253  C   LEU B 170      29.976  31.742   8.088  1.00 16.04
B    C
ATOM   2254  O   LEU B 170      29.754  32.397   7.069  1.00 17.27
B    O
ATOM   2255  N   PHE B 171      30.748  30.663   8.104  1.00 15.59
B    N
ATOM   2256  CA  PHE B 171      31.418  30.173   6.905  1.00 17.71
B    C
ATOM   2257  CB  PHE B 171      32.313  28.978   7.271  1.00 18.23
B    C
ATOM   2258  CG  PHE B 171      33.023  28.355   6.093  1.00 23.19
B    C
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ATOM   2259  CD1 PHE B 171      32.324  27.606   5.147  1.00 25.08
B    C
ATOM   2260  CD2 PHE B 171      34.395  28.521   5.930  1.00 25.84
B    C
ATOM   2261  CE1 PHE B 171      32.982  27.031   4.053  1.00 26.30
B    C
ATOM   2262  CE2 PHE B 171      35.064  27.949   4.840  1.00 26.12
B    C
ATOM   2263  CZ  PHE B 171      34.353  27.204   3.902  1.00 25.36
B    C
ATOM   2264  C   PHE B 171      30.413  29.773   5.824  1.00 15.84
B    C
ATOM   2265  O   PHE B 171      30.545  30.158   4.657  1.00 15.02
B    O
ATOM   2266  N   MET B 172      29.411  28.991   6.207  1.00 15.66
B    N
ATOM   2267  CA  MET B 172      28.407  28.548   5.241  1.00 14.21
B    C
ATOM   2268  CB  MET B 172      27.505  27.484   5.859  1.00 14.82
B    C
ATOM   2269  CG  MET B 172      28.167  26.139   6.076  1.00 17.32
B    C
ATOM   2270  SD  MET B 172      28.576  25.335   4.523  1.00 19.02
B    S
ATOM   2271  CE  MET B 172      30.140  24.649   4.909  1.00 18.35
B    C
ATOM   2272  C   MET B 172      27.552  29.701   4.723  1.00 15.52
B    C
ATOM   2273  O   MET B 172      27.216  29.750   3.543  1.00 16.04
B    O
ATOM   2274  N   SER B 173      27.191  30.623   5.610  1.00 17.55
B    N
ATOM   2275  CA  SER B 173      26.368  31.766   5.225  1.00 19.47
B    C
ATOM   2276  CB  SER B 173      25.962  32.554   6.462  1.00 18.60
B    C
ATOM   2277  OG  SER B 173      25.085  31.797   7.272  1.00 20.37
B    O
ATOM   2278  C   SER B 173      27.123  32.671   4.262  1.00 21.94
B    C
ATOM   2279  O   SER B 173      26.551  33.201   3.303  1.00 22.14
B    O
ATOM   2280  N   LEU B 174      28.412  32.853   4.523  1.00 22.66
B    N
ATOM   2281  CA  LEU B 174      29.252  33.688   3.676  1.00 23.53
B    C
ATOM   2282  CB ALEU B 174      30.652  33.804   4.287  0.50 23.45
B    C
ATOM   2283  CB BLEU B 174      30.671  33.756   4.215  0.50 23.44
B    C
ATOM   2284  CG ALEU B 174      31.647  34.741   3.608  0.50 23.66
B    C
ATOM   2285  CG BLEU B 174      31.036  34.904   5.148  0.50 23.44
B    C
ATOM   2286 CD1ALEU B 174      31.128  36.165   3.669  0.50 23.07
B    C
ATOM   2287 CD1BLEU B 174      32.414  34.656   5.737  0.50 22.70
B    C
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ATOM   2288  CD2ALEU B 174      32.995  34.633   4.308  0.50 22.85
B    C
ATOM   2289  CD2BLEU B 174      31.012  36.205   4.367  0.50 23.54
B    C
ATOM   2290  C   LEU B 174      29.340  33.097   2.274  1.00 25.13
B    C
ATOM   2291  O   LEU B 174      29.225  33.814   1.282  1.00 25.73
B    O
ATOM   2292  N   ARG B 175      29.547  31.785   2.204  1.00 25.47
B    N
ATOM   2293  CA  ARG B 175      29.641  31.074   0.933  1.00 26.85
B    C
ATOM   2294  CB  ARG B 175      29.872  29.584   1.196  1.00 28.61
B    C
ATOM   2295  CG  ARG B 175      30.384  28.818   0.006  1.00 31.65
B    C
ATOM   2296  CD  ARG B 175      30.369  27.331   0.279  1.00 35.80
B    C
ATOM   2297  NE  ARG B 175      29.017  26.786   0.193  1.00 37.83
B    N
ATOM   2298  CZ  ARG B 175      28.317  26.731  -0.935  1.00 41.57
B    C
ATOM   2299  NH1 ARG B 175      28.849  27.183  -2.060  1.00 42.90
B    N
ATOM   2300  NH2 ARG B 175      27.084  26.238  -0.944  1.00 42.15
B    N
ATOM   2301  C   ARG B 175      28.365  31.264   0.101  1.00 26.48
B    C
ATOM   2302  O   ARG B 175      28.416  31.705  -1.049  1.00 27.29
B    O
ATOM   2303  N   ASN B 176      27.216  30.954   0.690  1.00 24.26
B    N
ATOM   2304  CA  ASN B 176      25.943  31.095  -0.010  1.00 25.29
B    C
ATOM   2305  CB  ASN B 176      24.831  30.435   0.798  1.00 22.74
B    C
ATOM   2306  CG  ASN B 176      24.682  28.972   0.469  1.00 24.13
B    C
ATOM   2307  OD1 ASN B 176      25.668  28.285   0.187  1.00 22.83
B    O
ATOM   2308  ND2 ASN B 176      23.447  28.479   0.503  1.00 20.65
B    N
ATOM   2309  C   ASN B 176      25.539  32.522  -0.348  1.00 26.76
B    C
ATOM   2310  O   ASN B 176      24.759  32.753  -1.276  1.00 26.72
B    O
ATOM   2311  N   ALA B 177      26.068  33.481   0.397  1.00 25.95
B    N
ATOM   2312  CA  ALA B 177      25.729  34.870   0.162  1.00 26.17
B    C
ATOM   2313  CB  ALA B 177      25.737  35.633   1.487  1.00 24.10
B    C
ATOM   2314  C   ALA B 177      26.663  35.550  -0.826  1.00 25.49
B    C
ATOM   2315  O   ALA B 177      26.275  36.511  -1.478  1.00 25.51
B    O
ATOM   2316  N   CYS B 178      27.879  35.033  -0.964  1.00 27.87
B    N
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ATOM   2317  CA  CYS B 178      28.862  35.671  -1.820  1.00 27.66
B    C
ATOM   2318  C   CYS B 178      29.271  34.977  -3.128  1.00 29.33
B    C
ATOM   2319  O   CYS B 178      29.732  35.666  -4.035  1.00 31.34
B    O
ATOM   2320  CB  CYS B 178      30.123  35.902  -0.991  1.00 27.05
B    C
ATOM   2321  SG  CYS B 178      29.912  37.031   0.419  1.00 25.07
B    S
ATOM   2322  N   ILE B 179      29.109  33.664  -3.245  1.00 30.95
B    N
ATOM   2323  CA  ILE B 179      29.490  33.008  -4.491  1.00 31.56
B    C
ATOM   2324  CB  ILE B 179      29.681  31.496  -4.309  1.00 32.47
B    C
ATOM   2325  CG2 ILE B 179      30.764  31.239  -3.275  1.00 34.45
B    C
ATOM   2326  CG1 ILE B 179      28.356  30.851  -3.899  1.00 33.65
B    C
ATOM   2327  CD  ILE B 179      28.408  29.343  -3.849  1.00 35.23
B    C
ATOM   2328  C   ILE B 179      28.441  33.220  -5.576  1.00 31.05
B    C
ATOM   2329  OT1 ILE B 179      27.279  33.539  -5.240  1.00 29.84
B    O
ATOM   2330  OT2 ILE B 179      28.806  33.043  -6.756  1.00 32.57
B    O
HETATM 2331  O   HOH W 201      27.297  23.446  24.432  1.00 10.44
W    O
HETATM 2332  O   HOH W 202      29.001  24.489  16.199  1.00 15.87
W    O
HETATM 2333  O   HOH W 203      11.736  25.818  21.510  1.00 19.00
W    O
HETATM 2334  O   HOH W 204      24.143  15.462  11.058  1.00 16.00
W    O
HETATM 2335  O   HOH W 205      13.986  10.421   2.897  1.00 47.98
W    O
HETATM 2336  O   HOH W 206       9.264  23.783  21.316  1.00 19.55
W    O
HETATM 2337  O   HOH W 207      26.417  26.497  21.231  1.00 16.89
W    O
HETATM 2338  O   HOH W 208      25.199  18.812  10.440  1.00 16.53
W    O
HETATM 2339  O   HOH W 209      27.671  14.819   7.534  1.00 15.58
W    O
HETATM 2340  O   HOH W 210      17.220  31.319  12.529  1.00 18.46
W    O
HETATM 2341  O   HOH W 211       7.763  15.191  13.315  1.00 16.34
W    O
HETATM 2342  O   HOH W 212      25.429  52.025  16.393  1.00 21.97
W    O
HETATM 2343  O   HOH W 213       4.366  14.026  -0.146  1.00 16.43
W    O
HETATM 2344  O   HOH W 214      30.378  15.252   8.290  1.00 17.71
W    O
HETATM 2345  O   HOH W 215      29.716  36.103  14.680  1.00 26.32
W    O
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HETATM 2346  O   HOH W 216      29.851  44.950  27.330  1.00 16.23
W    O
HETATM 2347  O   HOH W 217      25.965  42.188  -1.336  1.00 26.70
W    O
HETATM 2348  O   HOH W 218      32.742  40.348  23.501  1.00 19.93
W    O
HETATM 2349  O   HOH W 219      21.669  14.477  11.866  1.00 21.69
W    O
HETATM 2350  O   HOH W 220      34.189  40.928  21.191  1.00 21.11
W    O
HETATM 2351  O   HOH W 221      13.503  33.656  -0.622  1.00 21.91
W    O
HETATM 2352  O   HOH W 222      24.529  39.089  -2.108  1.00 22.69
W    O
HETATM 2353  O   HOH W 223      20.087  30.335  -0.404  1.00 26.82
W    O
HETATM 2354  O   HOH W 224      21.910  37.842  18.502  1.00 21.17
W    O
HETATM 2355  O   HOH W 225      19.543  26.452 -10.389  1.00 24.04
W    O
HETATM 2356  O   HOH W 226      15.561  31.685  14.681  1.00 45.81
W    O
HETATM 2357  O   HOH W 227      32.308  36.045  30.019  1.00 28.38
W    O
HETATM 2358  O   HOH W 228      17.729  31.816   1.688  1.00 18.99
W    O
HETATM 2359  O   HOH W 229      25.158  23.427  25.705  1.00 23.41
W    O
HETATM 2360  O   HOH W 230      27.991  29.102  19.752  1.00 20.66
W    O
HETATM 2361  O   HOH W 231       3.725  18.194  12.154  1.00 33.73
W    O
HETATM 2362  O   HOH W 232      37.621  42.067  21.510  1.00 27.85
W    O
HETATM 2363  O   HOH W 233      19.597  28.257  20.861  1.00 28.65
W    O
HETATM 2364  O   HOH W 234      20.056  40.743  13.648  1.00 32.86
W    O
HETATM 2365  O   HOH W 235      11.670  39.187   7.650  1.00 30.82
W    O
HETATM 2366  O   HOH W 236      18.418  33.049  20.243  1.00 26.85
W    O
HETATM 2367  O   HOH W 237      23.466  27.862  16.542  1.00 25.38
W    O
HETATM 2368  O   HOH W 238      36.544  43.733   3.953  1.00 24.65
W    O
HETATM 2369  O   HOH W 239      20.855  44.986  20.266  1.00 20.67
W    O
HETATM 2370  O   HOH W 240       6.104  33.041   6.261  1.00 34.43
W    O
HETATM 2371  O   HOH W 241      22.194  38.315  15.523  1.00 30.42
W    O
HETATM 2372  O   HOH W 242      26.322  47.696  12.361  1.00 28.82
W    O
HETATM 2373  O   HOH W 243      29.634  17.921   1.255  1.00 23.78
W    O
HETATM 2374  O   HOH W 244      12.805  39.529   5.415  1.00 48.81
W    O
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HETATM 2375  O   HOH W 245       9.624  26.277   4.198  1.00 24.30
W    O
HETATM 2376  O   HOH W 246       7.395  13.510   7.017  1.00 35.04
W    O
HETATM 2377  O   HOH W 247      30.410  33.686  14.273  1.00 21.60
W    O
HETATM 2378  O   HOH W 248      36.748  43.355  23.420  1.00 28.82
W    O
HETATM 2379  O   HOH W 249      19.550  13.720  10.528  1.00 21.91
W    O
HETATM 2380  O   HOH W 250      17.891  27.372 -12.427  1.00 32.70
W    O
HETATM 2381  O   HOH W 251      31.614  45.127  10.612  1.00 28.57
W    O
HETATM 2382  O   HOH W 252      36.318  24.599  24.398  1.00 27.35
W    O
HETATM 2383  O   HOH W 253      27.851  21.966  22.159  1.00 35.57
W    O
HETATM 2384  O   HOH W 254      12.195  26.188   3.549  1.00 21.42
W    O
HETATM 2385  O   HOH W 255      14.952  35.943   7.315  1.00 31.47
W    O
HETATM 2386  O   HOH W 256      25.476  31.892  15.021  1.00 42.15
W    O
HETATM 2387  O   HOH W 257      33.419  16.973   5.504  1.00 24.87
W    O
HETATM 2388  O   HOH W 258       2.676  21.388   9.316  1.00 35.75
W    O
HETATM 2389  O   HOH W 259      25.575  34.428  -3.222  1.00 39.98
W    O
HETATM 2390  O   HOH W 260      14.941  30.863  -2.385  1.00 26.04
W    O
HETATM 2391  O   HOH W 261      41.672  27.415  23.709  1.00 35.93
W    O
HETATM 2392  O   HOH W 262      18.136  30.604  21.993  1.00 31.10
W    O
HETATM 2393  O   HOH W 263      32.907  42.731  25.674  1.00 26.77
W    O
HETATM 2394  O   HOH W 264      21.328  33.022  -5.079  1.00 32.93
W    O
HETATM 2395  O   HOH W 265      28.052  12.336   6.540  1.00 22.14
W    O
HETATM 2396  O   HOH W 266       2.099  19.008   5.021  1.00 32.55
W    O
HETATM 2397  O   HOH W 267      29.794  31.341  25.289  1.00 32.81
W    O
HETATM 2398  O   HOH W 268      20.757  45.357  22.862  1.00 36.33
W    O
HETATM 2399  O   HOH W 269      18.249  16.829 -10.961  1.00 31.63
W    O
HETATM 2400  O   HOH W 270       5.371  13.454  -3.003  1.00 38.53
W    O
HETATM 2401  O   HOH W 271      29.440  31.283  29.531  1.00 42.43
W    O
HETATM 2402  O   HOH W 272      28.073  49.822  16.597  1.00 34.43
W    O
HETATM 2403  O   HOH W 273       9.569  37.651  14.685  1.00 41.67
W    O
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HETATM 2404  O   HOH W 274       3.582  23.223  -3.241  1.00 41.20
W    O
HETATM 2405  O   HOH W 275      39.303  37.931  25.088  1.00 35.26
W    O
HETATM 2406  O   HOH W 276      27.169  49.230  14.079  1.00 27.21
W    O
HETATM 2407  O   HOH W 277      17.385  35.595  -7.830  1.00 39.15
W    O
HETATM 2408  O   HOH W 278      36.093  19.433  19.171  1.00 57.03
W    O
HETATM 2409  O   HOH W 279      31.185  14.743  10.858  1.00 33.84
W    O
HETATM 2410  O   HOH W 280      16.886  31.999  -1.178  1.00 30.74
W    O
HETATM 2411  O   HOH W 281      23.320  12.684   6.853  1.00 38.74
W    O
HETATM 2412  O   HOH W 282      35.109  41.222  24.391  1.00 35.21
W    O
HETATM 2413  O   HOH W 283      43.171  19.919   0.844  1.00 31.45
W    O
HETATM 2414  O   HOH W 284      21.356  14.695  23.557  1.00 28.47
W    O
HETATM 2415  O   HOH W 285      24.661  10.570   6.602  1.00 45.63
W    O
HETATM 2416  O   HOH W 286       4.247  12.050   1.832  1.00 39.46
W    O
HETATM 2417  O   HOH W 287      40.280  39.948  24.240  1.00 33.27
W    O
HETATM 2418  O   HOH W 288      20.284  56.897   0.611  1.00 44.29
W    O
HETATM 2419  O   HOH W 289      23.310  31.108  15.564  1.00 38.31
W    O
HETATM 2420  O   HOH W 290      48.053  26.077  15.288  1.00 47.19
W    O
HETATM 2421  O   HOH W 291      12.020  16.304  20.731  1.00 28.99
W    O
HETATM 2422  O   HOH W 292      41.231  23.934   2.570  1.00 33.94
W    O
HETATM 2423  O   HOH W 293      18.669  11.706 -13.630  1.00 36.09
W    O
HETATM 2424  O   HOH W 294       8.109  34.730   7.563  1.00 39.26
W    O
HETATM 2425  O   HOH W 295      15.600  35.689  -4.228  1.00 41.15
W    O
HETATM 2426  O   HOH W 296      -4.142  24.573  20.605  1.00 42.87
W    O
HETATM 2427  O   HOH W 297      15.622  34.076  15.219  1.00 42.95
W    O
HETATM 2428  O   HOH W 298      38.169  40.792  23.402  1.00 45.01
W    O
HETATM 2429  O   HOH W 299      27.537  26.052  -3.736  1.00 52.95
W    O
HETATM 2430  O   HOH W 300      35.494  16.860  10.304  1.00 43.09
W    O
HETATM 2431  O   HOH W 301      41.551  21.663   1.380  1.00 36.94
W    O
HETATM 2432  O   HOH W 302      45.225  29.031   6.035  1.00 40.03
W    O
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HETATM 2433  O   HOH W 303      31.772  47.636   4.279  1.00 35.07
W    O
HETATM 2434  O   HOH W 304      16.888  20.002 -11.152  1.00 39.19
W    O
HETATM 2435  O   HOH W 305      15.036  31.029  17.354  1.00 42.31
W    O
HETATM 2436  O   HOH W 306       8.035  38.484   2.278  1.00 36.39
W    O
HETATM 2437  O   HOH W 307       7.021   9.870  24.009  1.00 46.58
W    O
HETATM 2438  O   HOH W 308      -0.328  27.092  -6.529  1.00 39.32
W    O
HETATM 2439  O   HOH W 309      32.290  44.882  -6.224  1.00 41.91
W    O
HETATM 2440  O   HOH W 310      -2.886  27.829   1.400  1.00 46.46
W    O
HETATM 2441  O   HOH W 311      45.080  21.111   1.259  1.00 43.31
W    O
HETATM 2442  O   HOH W 312      34.187  18.021  11.951  1.00 33.37
W    O
HETATM 2443  O   HOH W 313      42.013  42.835  15.912  1.00 35.29
W    O
HETATM 2444  O   HOH W 314      21.506   9.309   4.752  1.00 35.56
W    O
HETATM 2445  O   HOH W 315      33.745  38.255  30.145  1.00 42.37
W    O
HETATM 2446  O   HOH W 316      26.849  28.079  -7.783  1.00 42.24
W    O
HETATM 2447  O   HOH W 317      22.190  18.955  -5.896  1.00 44.87
W    O
HETATM 2448  O   HOH W 318       5.056  11.251  -3.217  1.00 43.78
W    O
HETATM 2449  O   HOH W 319      30.465  47.010  -8.187  1.00 60.12
W    O
HETATM 2450  O   HOH W 320      25.131  34.069  -7.705  1.00 40.30
W    O
HETATM 2451  O   HOH W 321      -1.120  23.587   2.285  1.00 57.54
W    O
HETATM 2452  O   HOH W 322      27.796  32.147  25.994  1.00 52.28
W    O
HETATM 2453  O   HOH W 323       2.796  19.619  -4.238  1.00 43.84
W    O
HETATM 2454  O   HOH W 324       4.253  33.074   8.597  1.00 38.14
W    O
HETATM 2455  O   HOH W 325      28.162  22.354  26.470  1.00 46.35
W    O
HETATM 2456  O   HOH W 326      17.658  41.562  -4.831  1.00 45.26
W    O
HETATM 2457  O   HOH W 327      12.525  24.278  23.101  1.00 49.33
W    O
HETATM 2458  O   HOH W 328       1.417  20.936  21.185  1.00 51.98
W    O
HETATM 2459  O   HOH W 329       5.110  34.325   4.685  1.00 47.55
W    O
HETATM 2460  O   HOH W 330      23.854  24.173  -8.875  1.00 53.09
W    O
HETATM 2461  O   HOH W 331      26.863  30.894  27.666  1.00 47.65
W    O
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HETATM 2462  O   HOH W 332      32.534  14.831   7.143  1.00 39.84
W    O
HETATM 2463  O   HOH W 333      15.358  12.945  -2.666  1.00 37.81
W    O
HETATM 2464  O   HOH W 334      44.680  33.725  22.138  1.00 49.77
W    O
HETATM 2465  O   HOH W 335      12.020  38.120  13.522  1.00 58.79
W    O
HETATM 2466  O   HOH W 336      42.127  30.661  -3.910  1.00 44.39
W    O
HETATM 2467  O   HOH W 337       1.727  20.705   6.878  1.00 45.75
W    O
HETATM 2468  O   HOH W 338      -0.384  35.128  -7.818  1.00 49.01
W    O
HETATM 2469  O   HOH W 339      21.057  43.781  28.030  1.00 40.90
W    O
HETATM 2470  O   HOH W 340      11.861   9.923   3.834  1.00 41.37
W    O
HETATM 2471  O   HOH W 341      37.937  37.279  28.479  1.00 59.04
W    O
HETATM 2472  O   HOH W 342       6.363  12.922  12.257  1.00 43.48
W    O
HETATM 2473  O   HOH W 343       2.799  32.430  24.168  1.00 60.02
W    O
HETATM 2474  O   HOH W 344      29.796  50.785   1.614  1.00 53.08
W    O
HETATM 2475  O   HOH W 345      -0.874  32.698  -7.319  1.00 39.33
W    O
HETATM 2476  O   HOH W 346      36.654  46.102  -3.751  1.00 49.64
W    O
HETATM 2477  O   HOH W 347      22.253  20.580  21.775  1.00 38.38
W    O
HETATM 2478  O   HOH W 348      23.536  39.353  28.221  1.00 50.03
W    O
HETATM 2479  O   HOH W 349      21.979  23.483  27.337  1.00 56.78
W    O
HETATM 2480  O   HOH W 350      15.688   9.390   6.304  1.00 39.68
W    O
HETATM 2481  O   HOH W 351      17.446  31.911  24.017  1.00 49.08
W    O
HETATM 2482  O   HOH W 352      20.424  32.203  -1.926  1.00 52.71
W    O
HETATM 2483  O   HOH W 353       7.374  38.066  19.040  1.00 52.43
W    O
HETATM 2484  O   HOH W 354      40.616  34.974  29.409  1.00 43.05
W    O
HETATM 2485  O   HOH W 355      13.964  28.600  20.763  1.00 45.36
W    O
HETATM 2486  O   HOH W 356      21.968  11.935   4.239  1.00 34.43
W    O
HETATM 2487  O   HOH W 357      40.741  40.054  -5.266  1.00 50.01
W    O
HETATM 2488  O   HOH W 358       1.011  22.226  10.873  1.00 47.98
W    O
HETATM 2489  O   HOH W 359      30.521  24.949  -3.484  1.00 51.24
W    O
HETATM 2490  O   HOH W 360      30.394  22.663  13.867  1.00 35.80
W    O
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HETATM 2491  O   HOH W 361       1.298  28.757  23.599  1.00 45.73
W    O
HETATM 2492  O   HOH W 362      10.037  16.429  -9.605  1.00 43.70
W    O
HETATM 2493  O   HOH W 363       2.342  16.995  19.296  1.00 53.29
W    O
HETATM 2494  O   HOH W 364      18.754  21.800 -12.588  1.00 56.18
W    O
HETATM 2495  O   HOH W 365      18.388  23.021  28.255  1.00 48.80
W    O
HETATM 2496  O   HOH W 366      12.812  40.928   2.593  1.00 50.81
W    O
HETATM 2497  O   HOH W 367      20.573  19.834  -9.838  1.00 49.46
W    O
HETATM 2498  O   HOH W 368       3.924  11.192   4.654  1.00 47.96
W    O
HETATM 2499  O   HOH W 369      23.969  20.116  -9.041  1.00 44.24
W    O
HETATM 2500  O   HOH W 370      40.480  32.964   1.998  1.00 52.22
W    O
HETATM 2501  O   HOH W 371      20.730  46.882  18.743  1.00 38.87
W    O
HETATM 2502  O   HOH W 372      29.891  46.902  11.620  1.00 41.85
W    O
HETATM 2503  O   HOH W 373      27.107  45.779  -9.724  1.00 49.81
W    O
HETATM 2504  O   HOH W 374      45.521  35.688   5.405  1.00 50.64
W    O
HETATM 2505  O   HOH W 375       8.631  12.370  10.753  1.00 41.87
W    O
HETATM 2506  O   HOH W 376      -1.414  24.184   8.066  1.00 45.18
W    O
HETATM 2507  O   HOH W 377      25.847  26.771  -9.623  1.00 50.58
W    O
HETATM 2508  O   HOH W 378      17.044  35.686  20.995  1.00 46.08
W    O
HETATM 2509  O   HOH W 379      31.859  30.020  27.009  1.00 44.41
W    O
HETATM 2510  O   HOH W 380      15.331  35.172  17.686  1.00 42.80
W    O
HETATM 2511  O   HOH W 381      30.163  27.844 -12.299  1.00 48.94
W    O
HETATM 2512  O   HOH W 382      26.459  20.674  25.974  1.00 50.90
W    O
HETATM 2513  O   HOH W 383      11.215  40.705  -7.869  1.00 44.77
W    O
HETATM 2514  O   HOH W 384      39.653  28.993  25.532  1.00 42.77
W    O
HETATM 2515  O   HOH W 385       8.320  22.025  23.135  1.00 40.98
W    O
HETATM 2516  O   HOH W 386      19.109  57.899   2.281  1.00 52.58
W    O
HETATM 2517  O   HOH W 387      23.211  31.034   3.809  0.68 12.76
W    O
HETATM 2518  O   HOH W 388      23.669  33.864   2.886  0.68 17.24
W    O
HETATM 2519  O   HOH W 389      22.013  32.823   3.876  0.68 32.76
W    O
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END

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[1] Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.

Table 5: Solvent exposed residues of hIL-22.[1]

Residue	Solvent Exposed Area ($Å^2$)[2]	Residue	Solvent Exposed Area ($Å^2$)
SER38	80.00	HIS39	131.00
ARG41	112.00	ASP43	91.00
LYS44	82.00	SER45	49.00
ASN46	46.00	GLN48	103.00
GLN49	91.00	PRO50	99.00
TYR51	124.00	ILE52	24.00
THR53	27.00	ASN54	81.00
ARG55	51.00	PHE57	69.00
MET58	51.00	LYS61	123.00
GLU62	70.00	SER64	42.00
LEU65	135.00	ALA66	53.00
ASP67	27.00	ASN68	141.00
ASN69	35.00	THR70	126.00
ASP71	142.00	VAL72	45.00
ARG73	141.00	LEU74	11.00
ILE75	18.00	GLY76	13.00
GLU77	159.00	LYS78	116.00
PHE80	39.00	HIS81	141.00
GLY82	60.00	SER84	49.00
MET85	131.00	SER86	103.00
GLU87	22.00	ARG88	53.00
TYR90	31.00	LYS93	20.00
GLN94	49.00	ASN97	40.00
PHE98	10.00	GLU101	113.00
GLU102	83.00	PHE105	86.00
PRO106	72.00	SER108	46.00
ASP109	113.00	ARG110	96.00
PHE111	23.00	GLN112	136.00
PRO113	78.00	TYR114	54.00
GLN116	79.00	GLU117	60.00
VAL119	16.00	PRO120	58.00
PHE121	13.00	ALA123	33.00
ARG124	157.00	LEU125	3.00
SER126	20.00	ASN127	114.00
ARG128	126.00	SER130	54.00
THR131	117.00	HIS133	105.00
ILE134	30.00	GLU135	195.00
GLY136	39.00	ASP137	102.00
ASP138	39.00	LEU139	73.00
HIS140	48.00	GLN142	115.00
ARG143	155.00	ASN144	27.00
GLN146	80.00	LYS147	109.00

LYS149	53.00	ASP150	53.00

Table 5: Continued[1]

Residue	Solvent Exposed Area (Å^2)[2]	Residue	Solvent Exposed Area (Å^2)
THR151	21.00	LYS153	127.00
LYS154	147.00	LEU155	37.00
GLY156	29.00	GLU157	104.00
SER158	32.00	GLU160	35.00
ILE161	11.00	LYS162	6.00
ALA163	11.00	GLY165	11.00
GLU166	15.00	ASP168	40.00
LEU169	38.00	MET172	86.00
SER173	15.00	ARG175	70.00
ASN176	112.00	ALA177	21.00
ILE179	89.00		
Total area of chain A:	7584.		

[1] Amino acid residues correspond to residues in human IL-22, SEQ ID NO: 2.
[2]Solvent exposed areas c